

Epidemiologic Evidence Strongly Indicates Age-Related Gender Differences in Total Neoplasias Burden

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ABSTRACT

The evidence is presented that clearly shows women's predisposition to neoplasias in general, especially in reproductive organs, in age categories related to fertile period. This evidence is compared with our previous data on anemias and cardiometabolic disorders in Southern region of Brazil. The conclusion is made on urgent necessity for further investigations of morbidity and mortality in life-course epidemiology as intrinsic part of DOHaD paradigm.

Keywords

Morbidity, Mortality, Neoplasia, Ontogeny.

Abbreviations

DOHaD: Developmental origins of health and disease, ISOAD: International Society on Aging and Disease, LA-DOHaD: Latin-American chapter of International Society for DOHaD, RS: Rio Grande do Sul, WHO: World Health Organization.

Introduction

This is our first work to be published in the journal dedicated almost exclusively to oncology and cancer research. The main reason for this crucial step is our sincere belief that the results obtain by us recently may help a lot by advancing conceptual knowledge in this important area.

However, as a matter of fact, our half a century scientific trajectory was already, at least partially, associated with studies of normal and neoplastic growth, beginning from investigations in vitro of growth-related processes of macromolecular (DNA, total RNA and protein) biosynthesis in primary cultures of liver and pituitary cells from rats of different age groups [1], continuing by exploration in vivo of somatic and organ growth in humans and experimental models of laboratory animals [2] and finally, in epidemiologic studies of several oncologic diseases in human populations [3,4].

This, probably somewhat strange combination can be easily explained by our long-dated involvement in the activities of International Society for DOHaD, since DOHaD paradigm has two main branches: life-course epidemiology and multidisciplinary investigations of the mechanisms of programming / imprinting phenomena *in vivo* and *in vitro*.

Really, during the last two decades we studied age-related morbidity and mortality, using several databases (DataSus, WHO mortality database, epidemiologic data from Argentina and Chile). These our investigations can be subdivided in two rounds: at first, we explored mainly the data close to millenium transition (1998-2007) [5,6] and just recently, also during the more recent chronologic period of 2008-2023 [7].

However, exactly at the onset of second round of our epidemiologic research we have obtained the data indicating that at least anemias may have their morbidity probably related to fertile period in women [8], with natural boundaries of menarche and menopause. On the other hand, oncologic evidence obtained by us in the first round of epidemiologic research was quite heterogeneous, forcing inevitable conclusion about the absence of evidence in favor of unique general scheme of aging [9], if to consider it as biological process provoking age-related increase in morbidity and mortality.

Therefore, we decided to use in present work an alternative

approach, by exploring total morbidity and mortality from all cancer types together, trying subsequently to subtract the data on neoplasias of reproductive organs in both genders.

Materials and Methods

As earlier, we used epidemiologic data obtained from National database called DataSus (SUS is Unique System of Healthcare in Portuguese), freely available on the website of Brazilian Ministry of Health. The proportional (or relative) morbidity and mortality were evaluated in three steps:

- 1) Extraction of raw data from DataSus database;
- 2) Their recalculation in percent of total morbidity and mortality;
- 3) Descriptive statistics in chronologic periods of 4 y and visualization of treated data in plots constructed by means of Excel software.

It is important that morbidity was evaluated by means of the number of hospitalizations. The available data include the evidence for 3 Brazilian states of Southern region, but because of their great similarity, only the results for the state of Rio Grande do Sul (RS) are presented here. For the sake of better clarity, the Figures show only arithmetic means, because standard errors of the mean were quite small (usually less than 1/10 of the mean).

Results and Discussion

As can be clearly seen on the Figures 1-4, morbidity and especially mortality from all the neoplasias taken together are increasing in advanced age groups, thus confirming that cancer in general is aging-related disease. However, according to Figures 5-8, feminine fractions of morbidity and mortality are higher in major part of fertile period in women (approximately 10-49 y of age).

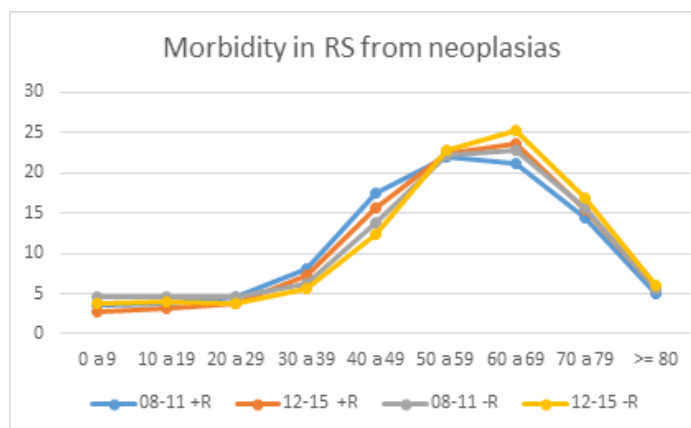


Figure 1: Morbidity from total neoplasias (+R) and without tumors in reproductive organs (-R) in the periods 2008-2011 and 2012-2015.

Here and on other Figures letter “a” between the years of age means the interval.

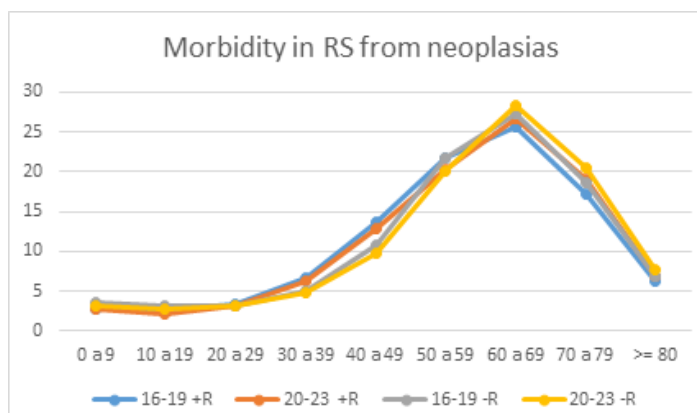


Figure 2: Morbidity from total neoplasias (+R) and without tumors in reproductive organs (-R) in the periods 2016-2019 and 2020-2023.

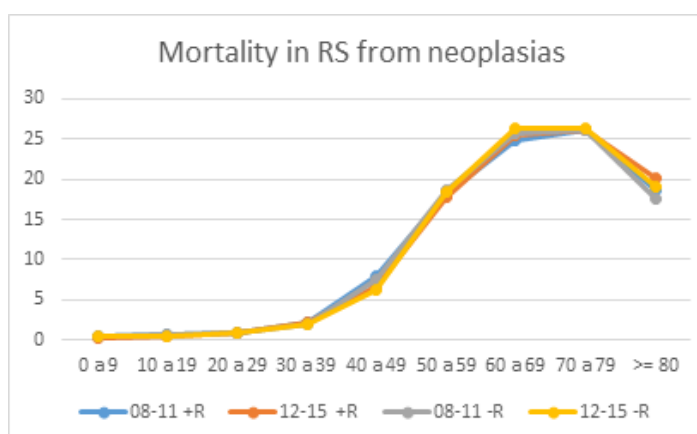


Figure 3: Mortality from total neoplasias (+R) and without tumors in reproductive organs (-R) in the periods 2008-2011 and 2012-2015.

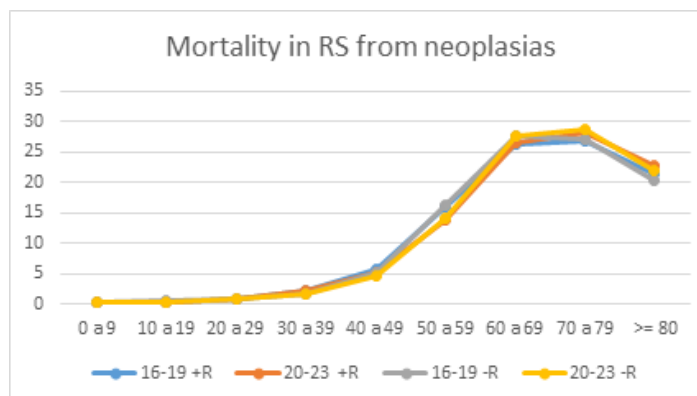


Figure 4: Mortality from total neoplasias (+R) and without tumors in reproductive organs (-R) in the periods 2016-2019 and 2020-2023.

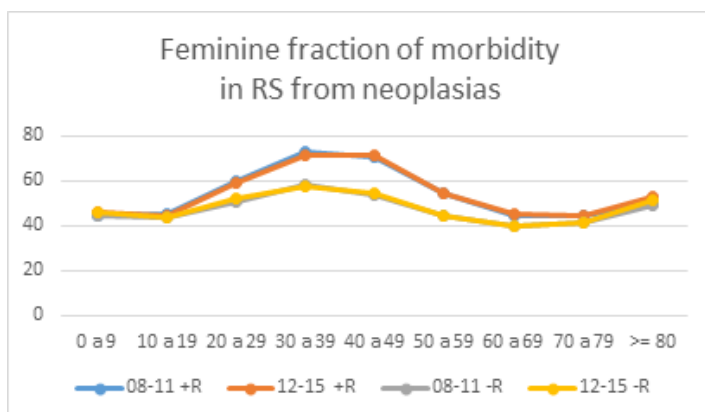


Figure 5: Feminine fraction of morbidity from total neoplasias (+R) and without tumors in reproductive organs (-R) in the periods 2008-2011 and 2012-2015.

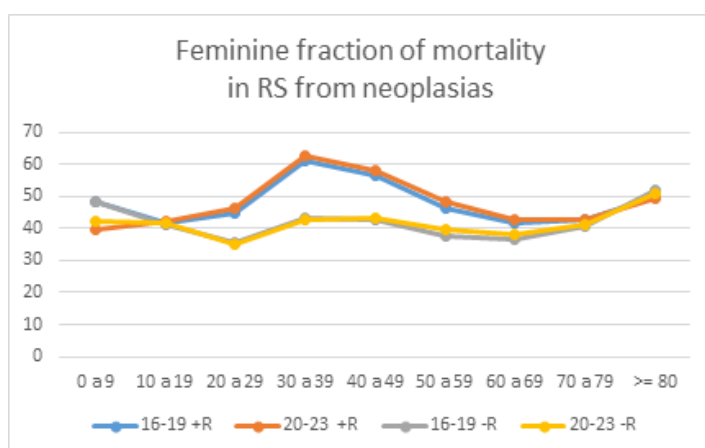


Figure 8: Feminine fraction of mortality from total neoplasias (+R) and without tumors in reproductive organs (-R) in the periods 2016-2019 and 2020-2023.

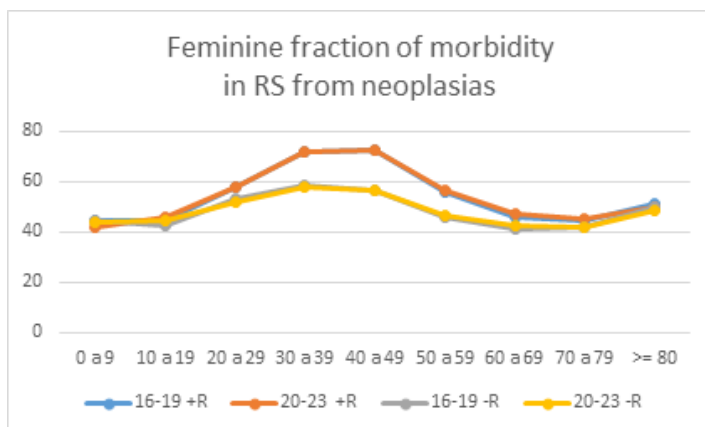


Figure 6: Feminine fraction of morbidity from total neoplasias (+R) and without tumors in reproductive organs (-R) in the periods 2016-2019 and 2020-2023.

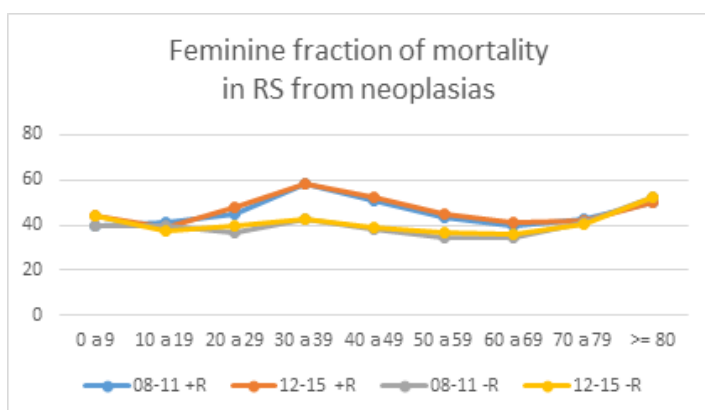


Figure 7: Feminine fraction of mortality from total neoplasias (+R) and without tumors in reproductive organs (-R) in the periods 2008-2011 and 2012-2015.

Nevertheless, the evaluation of total neoplasias morbidity and mortality except the tumors of reproductive organs (basically, breast and uterus in women, prostate in men and other reproductive organs in both genders) have demonstrated the diminished (but not completely) feminine fractions of morbidity and mortality, although without notable changes in age-related dynamics of epidemiologic indices.

On our opinion, these quite important results clearly show that women in general have different disadvantages in morbidity and mortality during their life (as compared to men) [10]: higher predisposition to anemias and also neoplasias, especially in reproductive organs, during fertile period and on the other hand, accelerated aging in postmenopausal phase, according to progressive increase in feminine fraction, at least for cardiometabolic disorders [11,12].

It is interesting that for neoplasias this phenomenon shows only a tendency, especially in mortality, but in fact, anemias do not demonstrated it almost at all. At present, it is not completely clear, how this difference in neoplasias and cardiometabolic disorders, together with anemias, can be explained.

We can only mention here, in a quite preliminary mode, that one of the reasons may be probably much lower involvement of stress and its mediators, first of all glucocorticoids, in the etiopathogeny of neoplasias and anemias, as compared to cardiometabolic disorders [13,14]. Moreover, the ontopathogenic model confronts much higher difficulties in explaining the involvement of corticosteroids in the phenomena of programming / imprinting of neoplasias, as compared, for example, to sex steroid hormones [15].

In conclusion, studies on age-related dynamics and gender differences of neoplasias and other diseases should be continued in various macroregions of the world, using other available databases. In addition, studies on molecular mechanisms of neoplastic growth

ought to pass much greater advances, but surely, it appears that higher functional activities of reproductive organs during fertile period in women should be taken into account.

This is especially important, if to remember that adverse events and pathologic processes in women are much more influential for offspring, therefore the health and well-being of present and future human generations may greatly depend on their consideration and prevention, well according to DOHaD paradigm.

Acknowledgement

This article is dedicated to the memory of outstanding Russian (and partially American) scientists with research activities on the borderlines between oncology, gerontology and endocrinology: Vladimir M. Dilman, his son Mikhail V. Blagosklonny and one of his colleagues, Vladimir N. Anisimov, all originally from St. Petersburg.

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