



## Women's Aging and Longevity: Some Lessons from the Onto- and Phylopathogenic Models

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### Abstract

Different types of sexual dimorphism are discussed for morbidity and mortality from age-related disorders and for longevity in general, as well as in relation to phylo- and ontopathogenic models in the framework of DOHaD concept.

**Keywords:** Aging; Longevity; Ontopathogeny; Gender Differences

### Introduction

At first we have to discuss the definitions. Aging is a biological process that results in increasing morbidity and mortality with advancing age, whereas longevity can be simply considered as inverse to mortality. Ontopathogeny is a continuous development of etiopathogenic mechanisms along the whole ontogeny, whereas phylopathogeny is a transfer of pathologic risk across generations [1].

There exist two types of aging: the first one is called successful (or healthy) and occurs almost without diseases, however its proportion is rather small (may be, much less than 30%). It means than another type of aging, pathologic one, surely predominates. On the other hand, morbidity and mortality attributed to senility as a code in the ICD-10 (International Classification of Disease, version 10) is less than 1%. Moreover, the majority of gerontologists is against an idea of considering aging as disease [2].

This short communication aims at briefly discussing our own experience, mainly with life-course epidemiology in the framework of DOHaD paradigm.

### Aging in both genders

It is already well known that mortality in humans is high shortly after birth and declines thereafter till the end of prepubertal period. For example, in Brazil the minimal values of mortality take place at the age of 9-10 y in both genders. From these ages onward the mortality steadily increases, especially from young adult period (20-29 y) [3].

It is important that gerontology is a science not only about senescence, but also on aging that apparently begins with conception, therefore gerontology can be considered as a science of the whole ontogeny [4].

From 2005, i.e. during the last 20 y we studied human morbidity and mortality, principally in the Southern region of Brazil [5,6]. It is essential to outline that morbidity was evaluated by us, according to the number of hospitalizations. Therefore, it is rather serious morbidity, not including ambulatory health care.

During these two decades we have investigated morbidity and mortality in various chronological periods, at first, several times for

the years 1998-2007 [5] and once for 2008-2014 [7], but recently also for 2008-2023 [8]. In all these cases we used raw epidemiologic data extracted from Brazilian national database called DataSus. Such data were recalculated to find relative (or proportional) morbidity and mortality for both genders together in each decade of age, as compared to the whole life-course values and thereafter we found feminine fraction, also in each decade of age, separately for 3 Brazilian states (provinces) of Southern region: Rio Grande do Sul (RS), Santa Catarina (SC) and Parana (PR).

Here we shall not describe all the evidence already mentioned in our previous Editorial [9], but only add some more data. First of all, the data clearly show the heterogeneity of morbidity and mortality, according to specific disorders, forcing us to make a conclusion about the absence of unique general scheme of aging [5]. Moreover, although at first the data on cardiometabolic disorders have allowed for our proposal about accelerated aging of women with onset of menopause [10,11], just recently the evidence on various types of anemias has not confirmed this proposal [8], but reinforced our previous conclusion on the absence of unique general scheme of aging [5].

In several preliminary investigations we evaluated seasonal rhythms of morbidity and mortality, as well as a gradient of mortality, according to socio-economic status (SES). In fact, we observed higher morbidity from respiratory disorders in the state of RS and higher general mortality in 3 Brazilian states of Southern region at winter season that in Southern hemisphere takes place inversely, as compared to Northern hemisphere [12,13]. Moreover, we have confirmed the existence of partial gradients of mortality, according to the number of years spent for education that roughly corresponds to SES [14].

### Women's aging and longevity

Our life-course epidemiological data have clearly shown that morbidity and mortality from cardiometabolic disorders in women increase during the age decades of 50-79 y, i.e. shortly after the onset of menopause [10,11]. Especially striking were the data on acute myocardial infarction, since before the age of 50 y there was a huge masculine predominance of this life-threatening disease, whereas after this threshold age the women became quite susceptible to it also. As an explanation of this peculiarity, earlier we tried to use the capacity of estrogens to act as antistress,

antioxidant and neuroprotective agents that obviously takes place almost exclusively during the whole fertile period in women (10-49 y).

On the other hand, the morbidity from affective diseases (depression, pathologic anxiety etc.) was higher in women during intermediate age categories (30-59 y), as compared to men [5], what roughly corresponds to 2-fold higher consumption of psychotropic drugs (antidepressants, benzodiazepine tranquilizers) by women in general [15], whereas there was a masculine predominance for schizophrenia in the same intermediate age categories.

It is important also that there existed high feminine predominance for cholecystitis in the intermediate age categories, whereas for men the peptic gastro-duodenal ulcer was much more characteristic [10]. The reasons for these types of sexual dimorphism are not clear, but we should attract attention to some recent suggestions about etiopathogeny of several non-communicable diseases. For example, atherosclerosis may be caused by intracellular bacteria, such as *Chlamydia pneumoniae* that probably can infect the fetus already from pregnant mother. On the other hand, gastro-intestinal ulcer (and perhaps cholecystitis also) may be related to infection by *Helicobacter pylori* that is highly prevalent in humans, since almost half of population may have this long-lasting disease, at least in cryptic form [16].

All these pieces of evidence may serve as partial explanation for heterogeneity of morbidity and mortality in human populations in a life-course mode.

### Conclusion

One of the most puzzling phenomena is greater longevity in women, as compared to men, that was a topic of several epidemiological investigations. In this regard, we would like to mention that long time ago it was already suggested by V.A. Geodakian that two genders appeared in evolution, in order to provide higher masculine involvement in risky activities, whereas for women the important role of transferring the accumulated experience to offspring was established. Obviously, this transfer is the essence of underlying mechanisms in onto- and phylopathogenic models, as our recent article in this journal also suggests [17].

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