Amerindian genetic ancestry as a risk factor for tuberculosis? Critical perspectives and implications for public policies in indigenous peoples’s health

Currently, the concept of vulnerability occupies a central space in debates on the health of indigenous peoples on a global scale, being widely referred to in discussions about the spread of the COVID-19 pandemic. This concept is present in the National Healthcare Policy for Indigenous Peoples in Brazil, which is aligned with the perspective of social determinants of health. In this interpretive scheme, which is central to public policies in many countries of the world, including Brazil, any disease that affects human populations involves, to some extent, biological aspects; however, the main determinants of disease and death of populations are considered to be primarily linked to ethnic, political and socioeconomic inequalities.

However, in the case of the health of indigenous peoples, arguments are sometimes advanced that are anchored in what we could call the other “side of the coin” of the concept of vulnerability. This is when the notion is based, predominantly – or completely – on arguments related to genetic determination. We want to comment here on a recent article published in *PLoS One* by Leal et al., which seems to us to be particularly illustrative of an emphasis that, mistakenly, sidelines the perspective of social determinants in the field of the health of indigenous peoples. It is a specific study on risk factors for tuberculosis, but it can be used as an example of a given way of doing (or not doing) science, with direct implications on health care practices and policies.

Leal et al. argue that “...AMR [Amerindian] genetic ancestry in the susceptibility to TB infection of a highly admixed Amazonian population...”. The investigation focused on the characterization of genomic ancestry profiles by comparing two groups: the first group consisted of 280 tuberculosis patients treated at a public hospital in Belém, Pará State; the second group consisted of 138 employees of the same hospital who had contact with tuberculosis patients in the last five years but did not become ill. Surprisingly, without controlling for socioeconomic variables, whose effects on tuberculosis disease are well known, the main conclusion of the study is as follows: “...AMR [Amerindian] ancestry in the 20% to 60% range was a risk factor for susceptibility to TB...” (p. 5). What would be expected as a central aspect of the methodology, certainly no less relevant for explanatory purposes than the genetic characterization itself, is indicated as limitation of the investigation: “...the study was unable to obtain sufficient data related to socioeconomic factor, cigarette smoking, alcohol consumption, in order to perform a stratified analysis” (p. 6).

In our evaluation, among the methodological aspects that compromise the internal validity of the results presented by Leal et al., is the strategy for the selection of controls, which in principle...
should seek representation of the population that generated the cases. In general, this is achieved by selecting neighbors of patients or hospitalized patients with other diseases. It does not seem to us that employees of the hospital in which the study was conducted, very possibly quite differentiated from the socioeconomic standpoint, living conditions and exposure to risk factors for tuberculosis, constitute a valid approximation of the underlying (hypothetical) cohort that generated the cases. In addition, the prerequisite of having had contact with patients with active tuberculosis for five years or more, without symptoms and diagnosis of tuberculosis, may have selected a different comparison group in relation to the characteristics of interest for the analysis of the (genomic) ancestry influence. Thus, the control group may have been mischaracterized as a reference for comparison with the cases, leaving the study vulnerable to selection bias.

Another relevant aspect is the management of covariates whose association with the risk of becoming infected and becoming ill with tuberculosis is well known and which were not considered in the analysis. The authors noted the insufficiency of some of these data as a study limitation, as already mentioned, but disregarded that part of the effect attributed to the “Amerindian ancestors” can be precisely explained by the differences in the cases and controls in relation to socioeconomic factors, among others. Considering all the limitations of the analysis presented and other deficiencies of the article, it is not possible to conclude that Amerindian ancestry constitute a risk factor for tuberculosis disease.

There is an additional element of context that should be mentioned: in the same journal in which the article by Leal et al. was published, there are other articles about the determinants of tuberculosis, which are also based on a case-control design, focusing on the social determinants of health. In line with what has been shown in numerous investigations in various parts of the world, one of these studies, which was conducted in Iraq, identified the following variables as risk factors for tuberculosis: age, household characteristics (such as number of windows), history of hospitalization, presence of coresidents who had tuberculosis, illiteracy, low household income, smoking, and absence of a BCG vaccination scar. What is indicated as a limitation in Leal et al. in the Iraqi study, which we mention here because it has several parallels and was published in the same journal, is at the heart of the elements identified as composing the risk factors for contracting tuberculosis. In this context, it is worth noting that there are several studies on the epidemiology of tuberculosis in indigenous communities in Brazil that point to the serious problems generated by the low quality of health services provided.

From a historical perspective, the tense relationship between biologizing explanations vis-à-vis the emphasis on socioeconomic and political dimensions has been part of the debates on the health of indigenous peoples in Brazil for a long time. In the second half of the twentieth century, there was an intense discussion about the relationship between the occurrence of infectious diseases and their relationship with the genetic characteristics of indigenous populations. At a time when measles epidemics affected numerous indigenous populations in the Amazon region, which had been recently contacted in the context of the violent expansion of economic and demographic fronts, researchers in the fields of health and genetics held debates with profound sociopolitical and health implications. Would the high mortality observed in indigenous populations be, to some extent, due to their inherited biological characteristics, in particular their genetic makeup that would confer an immune response below that observed in other human populations?

At the time of these discussions, which often took place in the pages of important international journals, the late geneticist James Neel, a recognized expert in the genetics of Amazonian indigenous populations, criticized the arguments about the greater biological susceptibility of indigenous peoples to epidemics of infectious diseases. The main point argued by Neel referred to the low density and methodological inconsistency of the scientific evidence to support such hypotheses. In Neel’s perspective, “...given the methodological difficulties involved in carrying out any systematic study of the question and the absence of convincing evidence in the literature, it was better to assume that genetic susceptibility was not the major influencing factor” (p. 447).

Genetic research is a subject of concern regarding the ethical implications associated with it worldwide. In Brazil, these concerns even generated a specific regulation, Resolution CNS 340/2004. Research ethics is seen by many researchers only as the need to respect the ethical principles proposed by the Belmont Report of 1978 and the rules derived from it. In the case of population genetics...
research, however, the possible consequences of these studies must be considered, especially when
their methodological design is open to criticism regarding accuracy. The greatest risk in the dissemina-
tion of information that is not the result of methodologically well-guided research is the possibility
of stigmatizing populations in the context of society in general, as already warned by United Nations
Educational, Scientific and Cultural Organization (UNESCO) in 1995, through its subcommittee on
Bioethics and Human Population Genetics: “Public attitudes to population genetics are often biased by social
ideologies, racism, and eugenics, and can lead to stigmatisation (as when population groups in which there is a
high incidence of genetic disease are selected for scientific investigation) and genetic reductionism” 12.

Specifically, in the case of indigenous peoples in Brazil, as well as in other parts of the world 13,
arguments regarding “reduced genetic resistance” have already been used to explain the higher lev-
els of disease and death in indigenous populations. This can be exemplified by the arguments of an
article published in 1977 on indigenous health policies and whose authors involved employees of the
Brazilian National Indian Foundation (FUNAI), which reads: “...the observed experiences demonstrate
their reduced genetic resistance to viral diseases (...) that a simple viral infection – flu, measles, smallpox, etc. –
can destroy up to 90% of the demographic contingent of these groups” 14 (p. 180). In contrast to the notions
of “genetic fatalism” in the face of the occurrence of infectious diseases, several other authors have
argued that the provision of adequate medical resources, in itself, was able to significantly reduce
mortality rates 10, thus deprivatizing the question of a possible greater genetic susceptibility of the
indigenous peoples.

In the book The Dialectical Biologist, Levins & Lewontin 15 (p. 4) write the following: “To do science is
to be a social actor engaged, whether one likes it or not, in political activity. The denial of the interpenetration
of the scientific and the social is itself a political act, giving support to social structures that hide behind scientific
objectivity to perpetuate dependency, exploitation, racism, elitism, colonialism”. This is even more so in the
case of vulnerable populations, such as indigenous peoples and other ethnic-racial minorities 16, when
health research does not consider aspects widely known to be related to disease outcomes (whether
tuberculosis or any other morbidity) in their respective methodological designs. In regard to health,
assigning a primacy in the explanatory chain to the genetic dimension without due consideration of
social determinants can be a way to justify the unacceptable.

There are abundant examples of how perspectives on the “fragility” or “strength” of bodies,
usually of ethnic-racial minorities, can lead to situations with direct implications for health care.
In the key to structural racism, potentially internalized by health professionals, there is a growing
literature that shows shocking situations, such as that of black patients who receive lower doses
of anesthetics, including at delivery, because they are perceived as having bodies supposedly more
resistant to pain 17. Similarly, in the absence of appropriate control of socioeconomic factors,
considering that Amerindian genetic ancestry in itself confers greater risk to tuberculosis can feed
views and perspectives in the routines of daily health professionals that take the focus away from
recognized central aspects in disease and death, i.e., marginalization conditions, precarious hous-
ing, and less access to health services, among many others.

The aforementioned geneticist James Neel provided the following comment in one of the debates
that took place decades ago during discussions on the biological aspects of indigenous peoples vis-à-
vis the response to epidemics of infectious diseases: not attributing to genetics without duly consid-
ering socioenvironmental determinants is a “position that would be ‘much less conducive to complacency’
on the part of health authorities” 11 (p. 447). Avoiding “complacency”, as stated by the geneticist, can be
interpreted as an alignment with the precautionary principle, clearly expressed in the field of the
regulation of research ethics in force in the country: “The researcher should always be aware of the risks
that the research can cause to the participants as a result of its procedures, and precautionary and protective
measures should be adopted to avoid damage or mitigate their effects” 18.

Unquestionably, investigations on the genetic-biological basis of infectious diseases in any
human population are part of a relevant research agenda. However, in the case of societies with such
a deep and cruel history of subjugation and marginalization, as is the case of indigenous peoples,
socioeconomic issues cannot in any way be relegated to a secondary level, even more so if subsumed
to “study limitations”. If there are such “limitations”, which are structurally so essential, perhaps it
is better not to publish the results because of the serious resulting biases. The damage may be of no little consequence.
Contributors


Additional informations

ORCID: Ricardo Ventura Santos (0000-0001-5071-443X); Luiz Antônio Bastos Camacho (0000-0003-4656-1914); Sergio Tavares de Almeida Rego (0000-0002-0584-3707); Luiz Eloy Terena (0000-0001-9073-6086); Ana Lucia Pontes (0000-0001-9162-5345); Jane Felipe Beltrão (0000-0003-2113-043X); Carlos E. A. Coimbra Jr. (0000-0003-4085-1080).

References


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