Paper prepared for the IUSSP conference, Tours 18-23 July 2005
S-144: Inequalities in Child Health and Mortality
Organiser : Godelieve Masuy-Stroobant

Overview on biological and behavioural factors of sex differences in child mortality in Africa

[Draft paper]

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Abstract

The paper provides an overview on biological and behavioural factors of sex differences in mortality, with emphasis on under-five children and on sub-Saharan Africa. The author argues that most differences in infant and child mortality are biological, since no consistent evidence exists of sex-specific discrimination in the African continent. The paper further develops cause specific biological differences, and argues that the list of diseases for which female mortality is higher than male mortality is limited. Findings are discussed in light of recent biological theories, and with different experiences in other continents.

Revised: 08/06/2005

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Introduction

Much has been written about sex differences in child mortality, though little has been formally demonstrated [Lopez and Ruzicka, 1983; Tabutin and Willems, 1995; Verburgge, 1989; United Nations, 1998, Waldron, 1983, 1987]. Most commonly in social sciences, cases of excess female mortality are interpreted as discrimination against females, assumed to be a cultural pattern, usually without documenting this discrimination. And conversely, cases of excess male mortality are attributed to genetic factors (male higher susceptibility to infectious and parasitic diseases, to non-communicable diseases, and to external causes), which are taken for granted for virtually any cause of death, except female specific diseases, such as breast cancer, cervix cancer, and maternal mortality. In this paper, where we focus on sub-Saharan Africa, we will argue basically the opposite, that is that cases of excess female mortality are rather due to biological factors, that the male disadvantage is not universal for infectious and parasitic diseases and that females have a strong disadvantage for certain infectious diseases and for auto-immune diseases.

The paper attempts at providing a synthesis of earlier work published elsewhere, based on an analysis of death rates and causes of death data, and on extensive fieldwork research in Niakhar, Senegal. The main argument is that, at least for sub-Saharan Africa, there is no evidence of discrimination against girls or boys in the fields of health, nutrition, and health care utilization. On the other hand, mortality as well as nutritional status vary by sex, and mortality by cause of death even more. In other continents, sex differences also vary by cause of death, from excess male mortality to excess female mortality, and they do vary according to level of mortality as well as a result of different causes of death profiles.

1. Biological and behavioural factors and the health transition

For overall mortality, as well as for selected causes of death, patterns of differences between groups (countries, social groups, gender, etc.) are usually attributed to either biological factors (nutrition, exposure to diseases, susceptibility, genetic factors) or to behavioural factors

(positive or negative attitudes, access and utilization of health services etc.) or a combination of both. A great variety of analysis has been conducted over the past century trying to account of observed differences in mortality.

With respect to sex differences, the most striking phenomenon has been the increasing gap between male and female mortality during the course of the health transition. For instance, in France, male and female life expectancy differed by only 1.2 years in 1860, as was the case since the beginning of the 19th century outside of war periods, and increased steadily for more than a century, reaching 8.2 years in 1980, date after which the difference tended to stabilize and even to decline. This change in sex differences in mortality is obviously related to the control of infectious and parasitic diseases, so central to the mortality decline over the same period of time. Therefore, the pattern of causes of death appears already as central in the debate about sex differences in mortality.

In his classic work on the health transition, Preston (1976) identified several causes of death and several age groups for which female mortality was higher than male mortality in high mortality populations. These differences tended to disappear at lower levels of mortality. Here again, sex differences appear as disease specific and age specific as well.

2. Proving that behaviour is causing sex differences

In order to formally show that behaviour is the main cause of sex differences in mortality, one needs three conditions to be fulfilled:

1. A documented differential behaviour between males and females;
2. The risky behaviour is associated with a risk of death higher than one (RR > 1);
3. The mortality fraction attributable to the risky behaviour corresponds to the excess mortality.

A typical case in developed countries will be alcohol or tobacco. Differential behaviour is easy to document by the mean annual consumption for males and females. Relative risks of deaths are known from longitudinal or case control studies, and the attributable risk can easily be computed. Excess male mortality from alcohol related diseases occurs despite higher female susceptibility for the same dose of alcohol intake, which shows the effect of behavioural factors (Bradley et al. 1998).

As far as we know this type of investigation has rarely been conducted among African children. In Asia however, a strong argument has been developed from case studies in India and Bangladesh: young girls are less fed than young boys, they have a lower nutritional status, and this lower nutritional status has an effect on excess female mortality (D'Souza and Chen, 1980; Das Gupta, 1987). In the Matlab studies, the risk of death from severe malnutrition was double for girls than for boys (Fauveau et al., 1990). If the first two conditions are well documented, we are not aware of any study documenting the whole pattern, in particular proper calculations proving the third condition, that is that differentials in nutritional status as a result of differential feeding explain all the sex differences in mortality, although this might well be true.

3. Behavioural factors and health outcomes in Africa

In a previous paper, using DHS surveys, we have documented that there is no evidence of differential behaviour between boys and girls in terms of preventive medicine, curative medicine and feeding practices in sub-Saharan Africa (Garenne, 2003). The proof here was given by comparing the distribution of the sex ratios of health indicators with the expected statistical distribution of these sex ratios assuming no differences in behaviour. Indeed, there was no difference at all between the observed and expected distributions. In contrast, the same 60 DHS surveys revealed a small excess of male mortality and somewhat more malnutrition among boys, which supports the idea of biological differences accounting for excess male mortality.

4. Proof that a disease might have differential effect on boys and girls

A formal proof that sex differences could be due to purely biological factors was given by an unfortunate experiment. While investigating the efficacy and safety of the Edmonston-Zagreb measles vaccine in Senegal, we found that the vaccine increased mortality, and that it was affecting girls more than boys (Garenne et al. 1991a,b). This was a randomized controlled trial, and there was no evidence of any bias in the randomization whatsoever. The same study was repeated in Haiti by a team from Johns Hopkins University, with the same vaccine and the same findings (Holt et al., 1993). Neither trial could formally prove the excess female susceptibility,

but the combination of the two trials was without doubt ($P < 0.017$). The vaccine was a live virus vaccine given at a very high titre, some 100 times the titre given in standard measles vaccines. The result was primarily the unexpected effect of high doses of a live virus on child survival. The effect could only be biological since it was a randomized controlled trial.

In Senegal, where the vaccine trial was conducted, natural measles, as well as whooping cough, showed consistently excess female mortality over the years ($RR = 1.51$, $P<0.01$ and $RR= 1.36$, $P< 0.11$). For other causes of deaths, male mortality among under five children was always higher than female mortality. Even though due to the small sample size excess female mortality from whooping cough was only borderline, it was significantly higher than for other causes of death. In addition, data on measles and whooping cough incidence allowed to precisely calculate case fatality rates, which was also much higher for girls than for boys, as expected since the incidence of these two diseases is basically the same for both sexes. Note that, like elsewhere in Africa, no evidence of any sex specific discriminatory health behaviour was ever found in this population (Garenne et al., 1991b).

Further investigation on natural measles mortality revealed an excess female mortality worldwide, at least among older children and young adults, and among children age 1-4 in many countries (Garenne, 1994). These could not reasonably be due to cultural factors, since excess female mortality was found in places as diverse as Southern Europe, Latin America, the Middle East and Japan. Available evidence also showed excess female mortality from whooping cough throughout the world, independent of cultural factors. This was known in the medical literature for a long time (Hewlett, 1990).

5. Investigation of sexist diseases

In another paper (Garenne and Lafon, 1997) we investigated diseases for which there was an excess female mortality among all causes of deaths available since 1950 and gathered by the World Health Organization (WHO). The list of infectious and parasitic diseases for which we found convincing evidence of excess female mortality below age 50 was short: three viral diseases (measles, smallpox, viral hepatitis), five bacterial diseases (whooping cough, streptococcal infections, diphtheria, cholera, paratyphoid), one parasitic disease

(ancylostomiasis), and two mycobacterial diseases (tuberculosis and leprosy). Among those, only a few caused excess female under-five mortality, the others being more lethal for women during the reproductive ages (15-44 years). No infectious disease in this list showed an excess female mortality above age 50 years.

Another proof of the importance of biological factors over behavioural factors in tropical countries is the case of malaria. Malaria is a disease easy to prevent (through mosquito nets, insect repellents, and chemoprophylaxis) and relatively easy to cure with antimalarial drugs, in particular with drug combinations. If there were strong behavioural factors in detriment of females, one would be likely to see excess female mortality from malaria in places where female discrimination is important. This is not the case, and we are not aware of any country in the world showing excess female malaria mortality. Available data show either no significant difference between the sexes, or excess male mortality from malaria.

6. Sexist diseases theory

In a paper entitled "Sexist diseases", we developed a theory on why some diseases might be more lethal for women, and why others are more lethal for men (Garenne and Lafon, 1997). The bottom line argument is that males and females have different hormonal systems, which have various effects on the way the immune system is reacting to infectious diseases. Animal models support this theory, a good example being that of Coxsackie's virus (Huber and Pfaeffle, 1994). The main mechanism seems to be the effect of sex hormones on the TH1/TH2 balance, and the deleterious effect of either excessive TH1 response, which seems to be more deleterious for males, or excessive TH2 response, which seems to be more deleterious for females. The list of diseases was limited (21 cases), however, these accounted for the most common infectious diseases causing death.

A strong argument in favour of our theory is also given by auto-immune diseases, which seem to be so much more prevalent and lethal among women than among men, risk ratios ranging form 2 to 1 to 10 to 1 and more for diseases such as systemic lupus erithematosus, idiopathic thrombocytopenic purpura or rheumatoid arthritis. Auto-immune diseases are

produced by abnormal and deleterious immune reactions, which seem to be related with sex hormones as well (Sarvetnick and Fox, 1990).

Another argument about the effect of TH1/TH2 balance on sex specific susceptibility to diseases has been given by another clinical trial. When supplementing infants with zinc in a rural area of Burkina Faso, we found a differential effect among boys and girls. Zinc is known to affect the TH1/TH2 balance, and we hypothesised that this was a similar phenomenon (Garenne et al., 2000).

7. Culture, causes of death and level of mortality

Much confusion has arisen from lack of distinction between levels of mortality, patterns of causes of death, and culture supposed to explain sex differences. For instance, a classic interpretation of excess female mortality in North African countries has been discrimination against little girls attributed to the Muslim culture. However, if one looks carefully, the same pattern of sex differences could be seen in "South Pattern" model life tables at the same level of mortality, which are primarily life tables from Southern Europe. For instance, in early Italian life tables, excess female mortality at age 1-4 years was consistent from 1881 to 1911 when infant mortality was above 150 per 1000, and disappeared later when mortality levels dropped dramatically, to become excess male mortality after 1921. (Preston, Keyfitz and Schoen, 1972). Excess female mortality was found in the 1960's in Morocco, Algeria and Tunisia at similar levels of infant mortality (above 140 per 1000), but was interpreted in a very different way (Tabutin, 1991).

Furthermore, Obermeyer and Cardenas (1997) did extensive studies of health seeking behaviours in North African countries, and did not find any evidence of discrimination against girls. This goes back to our first hypothesis: if no discrimination is found, how can we ascribe sex differences to discrimination?

A very interesting study was conducted in Sri Lanka, which has one of the longest series of deaths by age, sex and cause in the developing world since 1922. Langford (1984) showed that excess female mortality disappeared with declining mortality, in particular with the decline in hookworm mortality. Obviously the culture did not change over the period considered, but

only the pattern of causes of death and the level of mortality. According to our theory, if mortality from diseases causing excess female mortality declines faster than others, then excess female mortality should disappear or excess male mortality should increase. This seems to have been the case in Sri Lanka, as elsewhere in the world.

In a classic historical demography study, Poulain and Tabutin (1981) found excess female mortality for smallpox and whooping cough among young girls age 1-7 years in late 19th century and early 20th century Belgium, as well as excess female tuberculosis mortality among older girls and young women, age 7-21, whereas there was universal excess male mortality in infancy (below age 1 year), and excess male mortality for other causes in other age groups. Indeed, it would be surprising that parents would discriminate against boys for certain diseases, and against girls for other diseases. These effects are much more likely to be due to biological factors, and indeed the diseases with excess female mortality in ancient Belgium are in our list of "sexist diseases" with excess female mortality in the world.

Discussion

In this paper, we have focused on Africa, and quoted other studies from other parts of the world. In sub-Saharan Africa, we did not find any evidence of sex-specific discrimination in health seeking behaviour, neither did other authors working in North Africa. In sub-Saharan Africa, we did not find evidence of excess female mortality, though we did for selected diseases such as measles and whooping cough. Independent evidence indicates that this is most likely due to biological factors.

The idea that males have a higher susceptibility to any disease needs to be revised. Available data clearly show that males and females have comparative advantages for selected diseases. In high mortality populations, where communicable diseases such as tuberculosis, measles, whooping cough, smallpox and streptococcal infections are among the leading causes of death, the relative female advantage appears very slim, when not negative. When most infectious and parasitic diseases are under control, and largest causes of death are cardio-vascular diseases, cancers and external deaths, as in developed countries at the end of the 20th century, then the female advantage appears the largest, as shown by the large difference between male and female

life expectancy. However, if these causes of death are brought under control, and if auto-immune diseases become the leading causes of death, then female mortality might become higher than male mortality. If this scenario seems fiction at this point, in theory it could happen and is likely to have this effect. In other words, the balance between male and female mortality, as seen in demographic data, seems primarily determined by the cause of death profile and possible interactions between behaviour and disease (as for alcohol and tobacco), and only marginally by cultural factors.

It would be misleading to discount different findings from other parts of the world. However, so far, the only convincing pieces of evidence of discrimination against young girls which could have an effect on child mortality were from the Indian subcontinent, and primarily from India and Bangladesh. These countries have numerous atypical features, and a culture with many atypical behaviours often deleterious to females (sex selective abortion and infanticide, widow burning etc.). The rationale behind these behaviours is beyond the scope of this paper, and would require further exploration. However, these seem to be atypical behaviours, not found in other developing countries. Whether these are cultural patterns or patterns due to other causes, remains to be further explored.

Here we have emphasized on children and young adults, and infectious diseases primarily airborne and waterborne, for which exposure is usually similar for males and females. The case would be different for sexually transmitted diseases, for which age, gender and behaviours might interfere notably, as it is obviously the case for HIV/AIDS, and for STI's causing cervical cancers.

Disease epidemiology is complex, as well as disease immunology. These complex patterns are likely to reflect in the complexity of sex differences in mortality. Many diseases require further analysis. A major handicap for these studies is the sample size required for showing sex differences. If this is already an issue for demographic work, since small scale surveys are not enough, and larger data sets such as cause of death registration at national level are often needed for showing significant differences, this is even a stronger limitation for laboratory work, unless one could target fundamental pathological mechanisms. However, this has already been done for selected germs, and could be done in a larger scale.

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