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ASSOCIATION BETWEEN HEALTHY LIFE EXPECTANCY AT BIRTH AND CONSANGUINEOUS MARRIAGES IN 63 COUNTRIES

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Summary. In order to investigate the association between mean inbreeding coefficient (α) and healthy life expectancy at birth (HALE; years) the present ecological study on 63 countries was done. Statistical analysis showed that HALE negatively and positively correlated with $\log_{10}\alpha$ and $\log_{10}$GNI *per capita*, respectively ($p<0.001$). It should be noted that $\log_{10}\alpha$ and $\log_{10}$GNI *per capita* were significantly correlated with each other ($p<0.001$). After controlling for $\log_{10}$GNI *per capita*, significant negative correlations between $\log_{10}\alpha$ and HALE were observed. The countries were stratified according to their GNI *per capita* into low- and high-income countries. In countries with high income, after controlling for $\log_{10}$GNI *per capita*, the correlation between HALE at birth and $\log_{10}\alpha$ was significant (for males $r=-0.399$, df=32, $p=0.001$; for females $r=-0.683$, df=32, $p<0.001$). In high-income Asian and African countries, where consanguineous marriage is common, after controlling for $\log_{10}$GNI *per capita*, the correlation between HALE at birth and $\log_{10}\alpha$ was significant (for males $r=-0.819$, df=8, $p=0.004$; for females $r=-0.936$, df=8, $p<0.001$). It seems that consanguinity influences HALE independent of country income.

Introduction

Consanguineous marriage, a union between biologically related persons such as second cousins or closer relatives, has been a long-standing social habit among populations. The prevalence of consanguineous marriages depends on demographic, religious, cultural and socioeconomic factors (Bittles, 2001; Saadat, 2007, 2008). The inbreeding depression that results from consanguinity has a variety of known deleterious correlations with factors that affect health, fitness, morbidity and mortality within human populations (Bittles *et al.*, 1993; Stoltenberg *et al.*, 1999; Bittles, 2001; Saadat & Zendeh-Boodi, 2006). For countries such as Iran, where consanguineous marriage is common (Saadat *et al.*, 2004), the association between consanguinity and healthy life expectancy at birth is highly important for public health programmes. Therefore, the present ecological study was done.

Table 1. Mean of inbreeding coefficients, GNI *per capita* and sex-specific HALE at birth in the study countries

Country	GNI *per capita*	α (10^{-4})	HALE (male)	HALE (female)
Algeria	7640	152	62	63
Argentina	12,990	3	64	69
Australia	33,340	1	72	75
Bahrain	34,310	165	66	66
Bangladesh	1340	45	56	55
Belgium	34,790	3	70	74
Bolivia	4140	3	57	59
Brazil	9370	21	62	66
Burkina Faso	1120	355	42	43
Canada	35,310	4	71	75
Chile	12,590	6	67	72
China	5370	27	65	68
Colombia	6640	12	64	69
Costa Rica	10,700	11	68	71
Croatia	15,050	1	66	70
Czech Republic	22,020	1	68	72
Ecuador	7040	13	63	66
Egypt	5400	94	59	62
El Salvador	5640	14	58	63
France	33,600	2	71	76
Guinea	1120	131	46	48
Honduras	3620	11	61	64
Hungary	17,210	1	62	69
India	2740	238	56	57
Indonesia	3580	95	60	61
Iran	10,800	185	60	62
Iraq	3260	225	50	58
Ireland	37,090	1	71	74
Italy	29,850	4	73	76
Japan	34,600	13	73	78
Jordan	5160	200	62	64
Kuwait	49,970	205	69	69
Lebanon	10,050	91	60	64
Malaysia	13,570	47	62	66
Mexico	12,580	1	65	69
Mongolia	3160	63	55	62
Netherlands	39,310	1	72	74
Nigeria	1770	242	42	42
Norway	53,320	2	72	74
Oman	19,740	169	64	67
Pakistan	2570	282	56	55
Panama	10,610	6	65	68
Peru	7240	16	66	67
Philippine	3730	3	59	64

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Table 1. *Continued*

Country	GNI *per capita*	α (10^{-4})	HALE (male)	HALE (female)
Portugal	20,890	9	69	73
Saudi Arabia	22,910	223	61	64
Singapore	48,520	20	71	75
Slovakia	19,340	1	64	70
South Africa	9560	16	47	48
Spain	30,820	6	71	76
Sri Lanka	4210	92	61	65
Sudan	1880	197	50	50
Sweden	36,590	3	72	75
Syrian Arabia	4370	236	62	65
Tanzania	1200	236	45	45
Tunisia	7130	213	65	67
Turkey	12,350	74	64	67
UAE	44,340	223	68	68
UK	33,800	2	71	73
Uruguay	11,040	9	64	70
USA	45,850	1	68	72
Venezuela	11,920	7	64	68
Yemen	2200	215	53	55

Methods

Healthy life expectancy at birth (HALE; years) is defined as average number of years that a person can expect to live in 'full health'. Data about HALE for 2007 were obtained from the WHO website (http://www.who.int). The inbreeding coefficient is the probability that an individual has received both alleles of a pair from an identical ancestor. The mean inbreeding coefficient (α) values for different countries were obtained from the website http://www.consang.net. Several studies have shown that HALE correlates with income (Matthews *et al*., 2005; Gonzalez *et al*., 2010). The present study therefore used gross national income *per capita* (GNI; in international dollars) as a confounding factor. Data about GNI *per capita* for 2007 were obtained from the WHO website. Selection of countries was based on availability of the above-mentioned variables (Table 1).

Using the Kolmogorov-Smirnov test the GNI *per capita* and α did not show a normal distribution (for GNI *per capita*: Kolmogorov-Smirnov Z-test=1.579, p=0.014; for α: Kolmogorov-Smirnov Z-test=2.208, p<0.001). Logarithmic transformation was used on GNI *per capita* and α, because they had highly skewed distributions and the logarithmic transformations brought them closer to normal distribution (for $\log_{10}$GNI *per capita:* Kolmogorov-Smirnov Z-test=0.861, p=0.449; for $\log_{10}$α: Kolmogorov-Smirnov Z-test=1.133, p=0.153).

Correlations between the variables were determined using parametric Pearson's correlation coefficient analysis. Moreover, partial correlation coefficient analysis was done. Statistical analysis was performed using the Statistical Package for Social

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Table 2. Correlation coefficients between the study variables

Variable	df	HALE (male)		HALE (female)	
		r	*p*	*r*	*p*
Log_{10}GNI *per capita*	61	0.866	<0.001	0.850	<0.001
$Log_{10}\alpha$	61	−0.593	<0.001	−0.649	0.001
$Log_{10}\alpha$*	60	−0.263	0.039	−0.399	<0.001
$Log_{10}\alpha$**	32	−0.399	0.001	−0.683	<0.001
$Log_{10}\alpha$***	8	−0.819	0.004	−0.936	<0.001

*After controlling for Log_{10}GNI *per capita*.
**After controlling for Log_{10}GNI *per capita* in countries having GNI *per capita* at least $10,000.
***After controlling for Log_{10}GNI *per capita* in Asian and African countries having GNI *per capita* at least $10,000.

Sciences version 11.5 (SPSS Inc., Chicago, IL, USA). A probability of $p<0.05$ was considered statistically significant. For multiple comparisons the Bonferroni adjustment was applied. All statistical tests were two-sided.

Results and Discussion

Statistical analysis showed that HALE positively correlated with log_{10}GNI *per capita* (for males $r=0.866$, df=61, $p<0.001$; for females $r=0.850$, df=61, $p<0.001$). This finding confirmed previous studies (Matthews *et al*., 2005; Gonzalez *et al*., 2010). Also HALE showed negative correlation with $log_{10}\alpha$ (for males $r=-0.593$, df=61, $p<0.001$; for females $r=-0.649$, df=61, $p<0.001$). It should be noted that $log_{10}\alpha$ and log_{10}GNI *per capita* were significantly correlated with each other ($r=-0.885$, df=61, $p<0.001$).

Partial correlation analysis was carried out in order to eliminate the possible confounding effect of GNI *per capita* on the association between HALE and $log_{10}\alpha$. After controlling for log_{10}GNI *per capita*, significant negative correlations between $log_{10}\alpha$ and HALE were observed (Table 2). As shown in Table 2, the correlation coefficients between $log_{10}\alpha$ and HALE decreased after controlling for log_{10}GNI *per capita* in comparison with the correlation coefficients before controlling for the log_{10}GNI *per capita*. However, this change can partially be explained by the confounding effect of GNI *per capita* on the corrections. Table 2 also shows that correlation coefficients between HALE and $log_{10}\alpha$ (before and after controlling for log_{10}GNI *per capita*) were stronger for females than males. It is known that females have two X chromosomes and males have only one X chromosome. This difference may explain, at least in part, the effect of increasing the probability of homozygosity for loci located on the chromosome X in females due to parental consanguinity and/or difference(s) of environmental risk factors between males and females.

Countries were stratified according to their GNI *per capita*: low- and high-income countries with GNI *per capita* less than and more than $10,000, respectively. Statistical analysis showed that in high-income countries, after controlling for

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$\log_{10}$GNI *per capita*, the correlation between HALE and $\log_{10}\alpha$ was significant (for males $r=-0.399$, df=32, $p=0.001$; for females $r=-0.683$, df=32, $p<0.001$).

Since prevalence of consanguineous marriages is strongly associated with region (Bittles, 2001; Saadat *et al*., 2004; Othman & Saadat, 2009), further analysis was done using data for Asian and African countries. In high-income Asian and African countries, after controlling for $\log_{10}$GNI *per capita*, the correlation between HALE at birth and $\log_{10}\alpha$ was significant (for males $r=-0.819$, df=8, $p=0.004$; for females $r=-0.936$, df=8, $p<0.001$).

The problem with multiple comparisons is that the experiment-wise error rate is often much larger than the error rate applied to each single analysis. This can result in the declaration of spurious effects as significant. There are many procedures for adjusting the analyses to account for these multiple analyses. One of the simplest – a Bonferroni adjustment – requires that each analysis be carried out using an α/k Type I error rate, where $\alpha=0.05$ and k is the number of comparisons made (here $k=4$; $\alpha/k=0.012$). However, this results in a very conservative estimate of the statistical significance of each evaluation. Taken together, it might be concluded that consanguinity influences HALE independent of country income.

In countries where consanguineous marriages are common, increased levels of mortality and morbidity caused by the action of recessive and multifactorial traits can be predicted (Bittles, 2001). In most developing countries, socioeconomic circumstances have become more favourable. This has translated into advanced diagnostic and health care facilities. In these countries the incidence of non-genetic diseases has decreased dramatically. Because of the high prevalence of consanguineous marriages in these countries, genetic disorders now account for an increasing proportion of morbidity and death. Other studies are necessary in order to conclude that a large proportion of deaths can be attributed to inbreeding in several countries due to a high prevalence of consanguinity.

As mentioned in the Methods section, the data on GNI *per capita* and HALE were taken from publications in 2007, whereas the data on mean inbreeding coefficient listed in www.consang.net cover a much wider period (1950–2009). Since the GNI *per capita* of most developing countries has improved rapidly in recent years, direct correlation of these different data sets is the main limitation of the present study. The other limitation of the study is a potential bias called the 'ecological fallacy'. In ecologic study specific individuals are not studied, but rather groups of people are compared. Because nothing is known about exposures experienced by the groups (here homozygosity due to parental consanguineous marriages, family income, etc.), ecological studies may be more prone to biases that cannot be controlled. Also, consanguinity and GNI *per capita* may not be the only characteristics that can be distinguished between countries. There may be other confounding factors.

Finally, the present ecologic study raised the hypothesis that 'parental consanguineous marriages lead to higher mortality rates in offspring in comparison with unrelated marriages'. This hypothesis must be tested with more rigorous research.

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