Genetic Variations and their Association with Diseases among Kenyan Ethnic Populations

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SUMMARY

Human populations are polymorphic for many loci. The inhabitants of different regions of the earth can be characterised on the basis of the relative gene frequencies. These gene frequencies have been associated with certain characteristics such as disease and well being in general. This kind of relationship has not been exploited in many developing countries for the management and prevention of diseases. The aim of this study was therefore investigate the possible role genetics plays in disease, death and infections.

The mode of study involved a combination of a retrospective study and the analysis of genetic variation among Kenyan ethnic populations using ABO blood group system.

The results showed that there was association between allele frequencies of ABO system and disease and also mortality rates. It was also observed that populations which had high mortality rates many years back have also high infection rates of emerging diseases such as HIV. This study demonstrated that trends of mortality rates and HIV infection among Kenyan ethnic groups associated with allelic frequencies in ABO blood group system. Therefore understanding human genetics of a particular population is important in the management and prevention of diseases.

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Introduction

Although it has been suspected for a long time that individuals' responses to infection may have a strong genetic basis, it is only with advent of the molecular era that it has been possible to investigate this important possibility [1, 2]. Now several infections and diseases have been associated with various genes. Some of these are; sickle cell anaemia which has been associated with malaria [3], the relationship between HLA-DR polymorphism and the rates of clearance of hepatitis B virus [4], HIV infection resistance and Ckr-5 gene polymorphisms [5] and infection due to Pasteurella pestis and blood group ABO system [6]. Since there are genetic variations between populations, then certain diseases will be frequent in some populations while other populations may lack such diseases all together. For example sickle cell disease is very common among Africans and Tay - Sachs disease is common among Ashkenazi Jews. Also these genetic variations may be a predisposing factor for certain infections [7].

Most genetic variations are inherited hence it is possible to predict that sickle cell anaemia will be a major cause of childhood morbidity and mortality in sub-Saharan Africa so long as malaria will continue to be present in this region. Therefore if there is a certain condition or disease in a particular population then genetic factors should be implicated. Thus through an understanding of the molecular pathology of these conditions, better forms of treatment have been developed which have lead to a marked reduction in their frequency [8]. However detection of molecular factors responsible for many diseases is not yet established in many countries and in some may not be acceptable for religious and other ethical reasons. Thus the better management of

such diseases offers a major challenge to the field of medical practice especially in the developing countries. In view of this; this study was undertaken to identify the trends of infectious diseases and deaths among Kenyan ethnic populations and whether molecular markers may be used to follow such trends.

Methodology

This study was conducted at Provincial General Hospital in Nakuru, Kenya. The ethnic groups used for ABO blood typing were Luo, Luhya, Meru, Kisii, Somali, Kalenjin, Kikuyu and Kamba. Also for each ethnic group, average mortality rates for children under the age of five were calculated based on 1969, 1979 and 1989 Republic of Kenya population census [9,10,11]. Also HIV prevalence based on Central Bureau of Statistics of Kenya [12] was used for correlation analysis. The results were analyzed using student t-test; chi-square values, ChartWizard programmes and gene frequencies of ABO blood system (IA or allele A, IB or allele B and IO or allele O) were calculated using Bernstein method [13].

Results

The observed phenotype counts and the expected values for ABO blood groups in each ethnic group are shown in Table 1. The chi-square values are also presented in Table 1. From observed phenotype counts, gene frequencies in ABO blood group were worked out and are presented in Table 2.

From Table 1 it shows that all ethnic populations are in Hardy-Weinberg equilibrium, that is the observed frequencies do not significantly deviate from the expected frequencies. Also from Table 2, it is clear that different regions are represented by different genetic populations. For example Luhya have relatively high frequency for allele IA while Kisii and Meru have relatively high IB frequency. Kamba have low IA and IB frequencies. By average allele IA is the rarest in these populations.

Table 2: Gene frequencies in ABO blood group system in eight Kenyan ethnic groups

Ethnic group	N	Gene frequency		
		IA (allele A)	IB (allele B)	IO (allele O)
Luo	103	0.117	0.191	0.692
Luhya	52	0.239	0.179	0.582
Meru	20	0.163	0.256	0.581
Kisii	53	0.148	0.265	0.587
Somali	21	0.219	0.130	0.651
Kalenjin	56	0.197	0.132	0.671
Kikuyu	134	0.106	0.224	0.670
Kamba	45	0.092	0.154	0.754

The ethnic mortality rates for children under five years for the years 1969, 1979 and 1989 are tabulated in Table 3.

The mortality rates presented in Table 3 vary from one population to another. The genetic basis of this was sought by correlating the mortality rates with the frequency of the rarest allele in ABO blood group system. There was correlation between the frequency of allele IA and the mortality rates for the year 1969. This was the case with the years 1979 and 1989 as shown by scatter grams in Figure 1, 2 and 3. This shows that higher mortality rates are common in ethnic groups with higher frequency of allele IA.

Table 1: Observed phenotype counts and expected values for ABO blood group system in eight tribes of Kenya. X2 values are also shown.

Ethnic group	N	Observed phenotype count				Expected values				X^2	P
		A	B	AB	O	A	B	AB	O		(3 d.f.)
Luo	103	14	27	9	53	18	31	5	49	4.93	
Luhya	52	17	12	5	18	17	13	4	18	0.33	
Meru	20	4	7	2	7	4	7	2	7	0.00	
Kisii	53	7	17	8	21	10	21	4	18	6.16	<0.05
Somali	21	8	5	0	8	7	4	1	9	1.50	
Kalenjin	56	15	9	5	27	17	11	3	25	2.09	
Kikuyu	134	22	48	5	59	21	47	6	60	0.25	
Kamba	45	5	10	3	27	7	12	1	25	5.06	

Table 3: Child mortality rates per 1000 in three consecutive population censuses in the Republic of Kenya

Ethnic group	Mortality rates per 1000		
	1969	1979	1989
Luo	280	257	195
Luhya	196	187	110
Meru	132	104	60
Kisii	154	134	100
Somali	185	161	133
Kalenjin	199	165	90
Kikuyu	115	85	50
Kamba	172	151	80

From percentage of HIV prevalence in Kenya shown in Table 4, the correlation between HIV prevalence and mortality rates was worked out using student t-test. For 1969, t = 3.33; t = 3.21 for 1979 and t = 3.49 for 1989. All these showed that there was a significant correlation ($P < 0.02$) between HIV prevalence in 2003 and mortality rates in 1969, 1979 and 1989. The trends of mortality rates and HIV prevalence among ethnic groups are shown in Figure 4, 5 and 6.

Figure 1: Scattergram showing the association between the frequency of allele A and mortality rates among ethnic groups in 1969

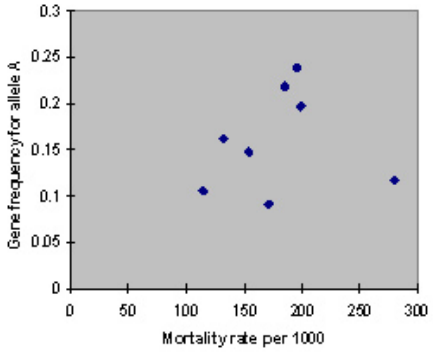


Figure 2: Scattergram showing the association between the frequency of allele A and mortality rates among ethnic groups in 1979

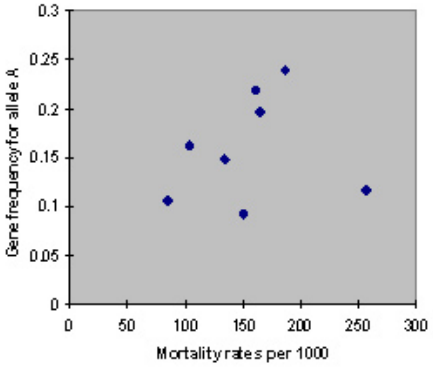


Table 4: Percentage of HIV prevalence among eight Kenyan ethnic groups with their corresponding serial numbers during the year of 2003

Serial No.	Ethnic group	% HIV prevalence
1	Luo	21.8
2	Luhya	6.8
3	Meru	3.7
4	Kisii	4.0
5	Somali	1.3
6	Kalenjin	3.4
7	Kikuyu	4.9
8	Kamba	5.4

The figures show that a population which had high mortality rates in 1969 also had high mortality rates in 1979 and 1989. Also they show that a population which had high mortality rates in 1969 is likely to have high mortality rates in 2003 due to HIV.

Figure 3: Scattergram showing the association between the frequency of allele A and mortality rates among ethnic groups in 1989

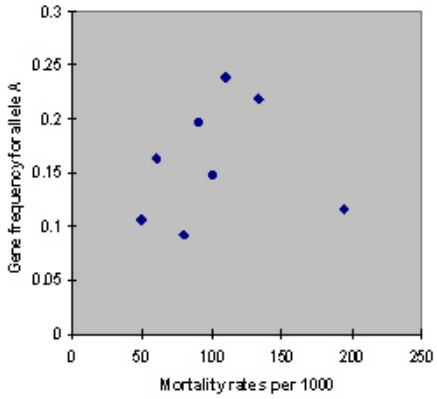


Figure 4: Correlation between Mortality Rates in 1969 and % of HIV Prevalence in 2003

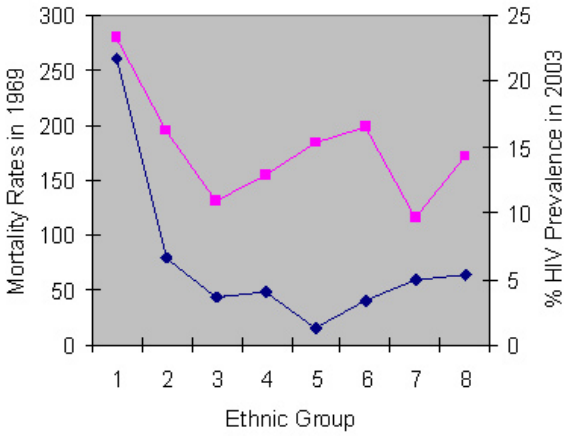


Figure 5: Correlation between Mortality Rates in 1979 and % of HIV Prevalence in 2003

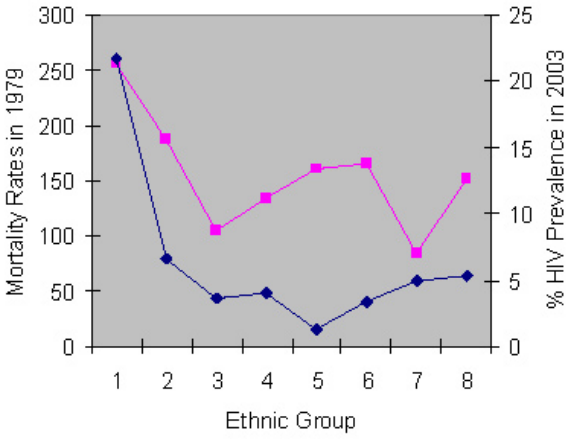
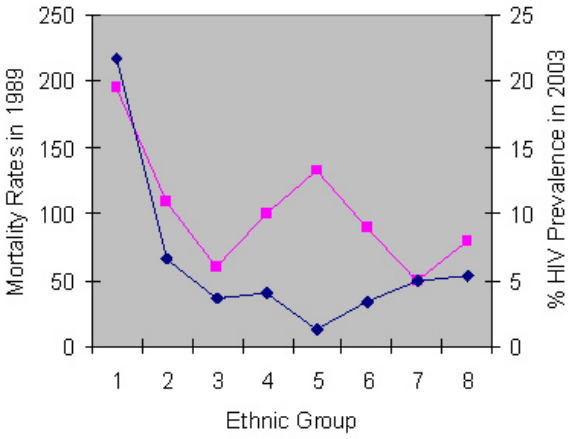


Figure 6: Correlation between Mortality Rates in 1989 and % of HIV Prevalence in 2003



Discussion

The results of this study showed that there are differences in the allelic frequency in the ABO locus among Kenyan ethnic groups (Table 2). Since blood group B is the rarest type in the whole human population, it has often been used to follow the migrations and mating among human populations [14]. According to this study, blood group type A was the rarest. This variation may be due to environmental factors since it has been demonstrated that allele frequencies of the ABO system vary more from one population to the next than do those of the MN and Rh systems [15]. It may also be due to natural selection reflecting some advantage against different forms of diseases.

From Figures 1, 2 and 3, there is some association between allelic frequencies in ABO system and diseases and hence mortality rates. ABO locus is not the only locus which may be associated with disease since there are several other loci which have been demonstrated to be associated with certain diseases. For example the gene encoding tumour necrosis factor-α (TNFα) is associated with increased likelihood of dying from cerebral malaria [16]. There are HLA-DR associations with a variety of parasitic illness including leishmaniasis, onchocerciasis and filariasis. TNFα polymorphisms have also been found to modify the course of meningococcal meningitis, hepromatous leprosy and tranchoma [17, 18, 19]. The immunoglobulin supergene family called ICAM-1 has a wide range of immunological functions and it has also been found to have an important role in adherence of P. falciparum-infected red cells in cerebral malaria. It has been found that, in parts of Africa, there is a high prevalence of a polymorphism of this protein which appears to be a predisposing factor for cerebral malaria. Increased susceptibility to bacterial infections has been related to several polymorphisms of the gene for the mannose-binding protein [20]. It has long been known that the ability to secrete the soluble form of ABO blood group antigens into the saliva and other body fluids may be associated with variable susceptibility to bacterial infections although this association is less strong than that of HLA loci and disease [21]. From these associations it is evident that genetic factors play an important role in the pathogenesis of diseases.

The significant correlation, in this study, between HIV infection in 2003 and mortality rates in 1969, 1979 and 1989 (Figures 4,5 and 6) implies that factors which led to higher mortality rates in the 60's, 70's and 80's are the same predisposing factors for HIV infection in 2003. The factors are mainly genetic since 1969 the Luo ethnic group had the highest mortality rates (Table 3) and the highest HIV infection in 2003 (Table 4). The Luo borders the Kisii, Luhya and Kalenjin but have very high HIV prevalence as they had mortality rates. This would imply that genetic factors influence susceptibility to diseases.

Conclusion

Molecular genetics has a great deal to offer tropical medicine in understanding the population genetics and dynamics of both infectious and non-infectious diseases. It is therefore important to understand the genetics of a population for better management and prevention of disease.

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