INTERNATIONAL JOURNAL OF LEPROSY Volume 34, Number 4
Printed in U.S.A.

ABO Blood Groups and Leprosy[1]

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Different research workers have studied a possible association between the incidence of leprosy and the distribution of blood groups in human populations and have come to different conclusions. The earlier workers Malaiholio (4), Marti (5) and Cesarino Netto (1), concluded that no relationship exists between the distribution of blood groups and increased incidence of leprosy. Later Weidmann and Katkin (7) studied the distribution of blood groups in relation to leprosy and believed there was no definite relationship between predisposition to leprosy and the blood grouping of the different races. Recently Hsuen and associates (3) concluded from their study that the distribution of blood groups in leprosy patients differs significantly from that of the general population, a fact, if true, suggesting an association between the incidence of leprosy and the ABO blood groups. In the investigation here reported an attempt has been made to study the problem with the help of data collected by the Central Leprosy Teaching and Research Institute, Chingleput, India.

METHODS AND MATERIALS

The aim of the present study is to determine if any association exists between the distribution of blood groups and the incidence of leprosy, or in other words to find out if individuals belonging to a particular blood group are more prone to the disease than others. The inheritance of these blood groups is controlled by three allelomorphic genes with certain frequencies in the normal population, which generally differ in different races. Most of the genetic variation between different populations is quantitative rather than qualitative. The variation is in the frequency of particular genes rather than in the possession of genes unique to them. The association between the distribution of blood groups and the incidence of leprosy, or in other words the greater affinity of individuals belonging to a particular blood group for leprosy, can be revealed only by a significant difference in the frequency of the gene controlling the inheritance of that particular blood group in the normal population as compared with that in the population of leprosy patients. Thus if there is any real association between the distribution of blood groups and the incidence of leprosy, the frequencies of the genes controlling the inheritance of blood groups should be different in a population of leprosy patients from those in the normal population free from leprosy. Only when these frequencies are different can we be sure of an association between the two.

Data have been collected by the Central Leprosy Teaching and Research Institute on the distribution of blood groups of lepromatous and nonlepromatous leprosy patients and the general population of normal persons. People with leprosy come to the Institute for treatment from different parts of South India. For practical purposes they can be taken as representative of the South Indian population. In addition, for comparison, data are considered on 70,000 persons, collected by the King Institute, Guindy, Madras (2), in their routine tests for blood bank purposes on the distribution of blood groups in the South. Details of the data collected as required for the present study are

[1] Received for publication April 29, 1966.

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given in Table I. Four groups are set up for comparison.

The next step was the estimation of gene frequencies. Among the three genes controlling the inheritance of the blood groups ABO the gene O is recessive to A and B. Let r, p, and q be the frequencies of the genes O, A, and B respectively. Under random mating the expected probabilities of the genotypes and the phenotypes with their derivatives with respect to the independent parameters p and q (since $p + q + r = 1$) will be:

Phenotype	Genotype	Probability		Partial derivatives	
				$\delta\pi$	$\pi\delta$
O	OO	r^2			
A	AA	p^2	$p^2 + 2\,pr$	δp	δq
	AO	$2\,pr$		$-\,2r$	$-\,2r$
B	BB	q^2	$q^2 + 2\,qr$	$2r$	$-\,2p$
	BO	$2\,qr$		$-\,2q$	$2r$
AB	AB	$2\,pq$		$2q$	$2p$

Let N be the total observed frequencies of all the phenotypes in any population. The rough estimates of the gene frequencies in any population are then as follows:

$$r^1 = \sqrt{\frac{O}{N}}$$

$$p^1 = 1 - \sqrt{\frac{O + B}{N}}$$

$$q^1 = 1 - \sqrt{\frac{O + A}{N}}$$

where $r^1 + p^1 + q^1$ should add up to unity.

The necessary corrections required to obtain the correct estimates of the gene frequencies are provided by using "the method of maximum likelihood" (method of scoring) ([6]). The variances of these estimates are also obtained. The method of estimating the gene frequencies, together with their variances in the four populations, is explained briefly in subsequent paragraphs.

ESTIMATION OF GENE FREQUENCIES

The observed frequencies of the four phenotypes in the four populations are given in Table 1. A rough estimate of the gene frequencies in the different populations is presented in Table 2.

According to the probability law the total should add up to unity. But from Table 2 it will be seen that the estimates need correction, since their totals do not add up to unity. The necessary corrections are provided by calculating the efficient scores. The probability and the necessary coefficients for calculating efficient scores at the approximate values of the gene frequencies in the different populations are given in Table 3.

TABLE 1. *Distribution of blood groups in different populations.*

Population	Blood groups				
	O	A	B	AB	Total
Lepromatous	339	166	227	50	782
Nonlepromatous	158	99	135	30	422
Normal[a]	473	291	369	75	1,208
South Indian	28,040	14,721	22,432	4,907	70,100

[a] Normal persons who were grouped in the Laboratory Division of this Institute.

TABLE 2. *Rough estimate of gene frequencies in different populations.*

Gene frequencies	Type of population			
	Lepromatous	Nonlepromatous	Normal	South Indian
r^1	0.65841	0.61189	0.62575	0.63246
p^1	0.14924	0.16675	0.16513	0.15147
q^1	0.19640	0.21961	0.20473	0.21897
Total	1.00405	0.99825	0.99561	1.00290

The scores on p and q are calculated by using the formulae

$$\phi p = \sum_{i=1}^{4} fi \left(\frac{1}{\pi} \cdot \frac{\delta \pi}{\delta p} \right)$$

$$\phi q = \sum_{i=1}^{4} fi \left(\frac{1}{\pi} \cdot \frac{\delta \pi}{\delta q} \right)$$

where f_i is the observed frequency of the i^{th} phenotype (i = 1.4). The scores are calculated in the four populations and are given in Table 4.

To provide the necessary corrections we need the information matrix and its inverse. The elements of the information matrix are calculated in all four populations with the help of data from Table 3, and given in Table 5. The elements of the information matrix are given by the formulae

$$I_{pp} = \sum \frac{1}{\pi} \left(\frac{\delta \pi}{\delta p} \right)^2$$

$$I_{qq} = \sum \frac{1}{\pi} \left(\frac{\delta \pi}{\delta q} \right)^2$$

$$I_{pq} = \sum \frac{\delta \pi}{\delta p} \left(\frac{1}{\pi} \cdot \frac{\delta \pi}{\delta q} \right)$$

The inverses of the information matrices are obtained by the Dolittle technic, and the elements are given in Table 6.

The necessary corrections for p and q can be calculated by using the following formulae

$$\delta p = \frac{I^{pq} \phi p + I^{pq} \phi q}{N}$$

$$\delta q = \frac{I^{pq} \phi b + I^{qq} \phi q}{N}$$

These corrections are either added or subtracted, whichever is the case, accordingly, from the rough esitmates to obtain a better estimate of the gene frequency. With these improved estimates the whole process is repeated until the corrections become negligible. In this particular problem two more iterations lead to negligible corrections. These iterations have been carried out and the final corrected estimates of the gene frequencies in the different populations are given in Table 7.

The elements of the inverse of the information matrices with these improved estimates are given in Table 8.

The variances of these estimated gene frequencies can be obtained from Table 8 and are given by the following formulae

$$V(_p) = \frac{I^{pp}}{N}$$

$$V(_q) = \frac{I^{qq}}{N}$$

$$V(_r) = \frac{I^{pp} + 2I^{pq} + I^{qq}}{N}$$

Variances of the estimated gene fre-

TABLE 3. *Calculations necessary for efficient scores.*

Population	Phenotype	Probability (π)	Coefficients for scores				Observed frequency (f)
			$\frac{\delta\pi}{\delta p}$	$\frac{1}{\pi}\cdot\frac{\delta\pi}{\delta p}$	$\frac{\delta\pi}{\delta q}$	$\frac{1}{\pi}\cdot\frac{\delta\pi}{\delta q}$	
Lepromatous	O	0.43350	−1.31682	−3.03765	−3.31682	−3.03765	339
	A	0.21879	1.31682	6.01865	−0.29848	−1.36423	166
	B	0.29720	−0 39280	−1.32167	1.31682	4.43075	227
	AB	0.05862	0.39280	6.70078	0.29848	5.09178	50
Nonlepromatous	O	0.37441	−1.22378	−3.26856	−1.22378	−3.26856	158
	A	0.23187	1.22378	5.27787	−0.33350	−1.43831	99
	B	0.31698	−0.43922	−1.38564	1.22387	3.86975	135
	AB	0.07324	0.43922	5.99700	0.33350	4.55352	30
Norma	O	0.39156	−1.25150	−3.19619	−1.25150	−3.19619	473
	A	0.23393	1.25150	5.34989	−0.33026	−1 41179	291
	B	0.29813	−0.40946	−1.37343	1.25150	4.19783	369
	AB	0.06761	0.40946	6.05620	0.33026	4.88478	75
South Indian	O	0.40000	−1.26492	−3.16230	−1.26492	−3.16230	28,040
	A	0.21454	1.26492	5.89596	−0.30294	−4.41204	14,721
	B	0.32493	−0.43794	−1.34780	1.26492	3.89290	22,432
	AB	0.06633	0.43794	6.60244	0.30294	4.56716	4,907

quencies in the different populations are calculated by using the above formulae, and given in Table 9.

TESTS OF SIGNIFICANCE

After estimating the gene frequencies and their variances, the next step is to see if the gene frequencies differ from population to population. This is done by application of the *t*-test. Tests of significance show that:

1. The frequencies of the genes controlling the inheritance of blood groups do not differ in samples of the general population grouped in the Institute and the South

TABLE 4. *Efficient scores in different populations.*

Scores	Type of population			
	Lepromatous	Nonlepromatous	Normal	South Indian
ϕp	4.33752	−1.07475	−7.56055	287.41000
ϕq	4.14372	−1.01832	−7.27079	279.95408

TABLE 5. *Elements of the information matrix in different populations.*

Elements of information matrix	Type of population			
	Lepromatous	Nonlepromatous	Normal	South Indian
I_{pp}	15.07674	13.70155	+13.73756	14.93970
I_{pq}	2.46324	2.54411	2.51445	2.50922
I_{qq}	11.76153	10.72298	11.33312	10.43266

TABLE 6. *Elements of inverse matrices in different populations*

Elements	Type of population			
	Lepromatous	Nonlepromatous	Normal	South Indian
I_{pp}	0.06868	0.07635	0.07587	0.06975
I_{pq}	−0.01438	−0.01811	−0.01683	−0.01678
I_{qq}	0.08804	0.09756	0.09197	0.09489

TABLE 7. *Corrected estimates of gene frequencies in different populations.*

Gene frequencies	Type of population			
	Lepromatous	Nonlepromatous	Normal	South Indian
r	0.65506	0.61344	0.62936	0.63009
p	0.14894	0.16692	0.16546	0.15125
q	0.19600	0.21964	0.20518	0.21866
Total	1.00000	1.00000	1.00000	1.00000

TABLE 8. *Elements of inverse matrices in different populations from improved estimates.*

Elements	Type of population			
	Lepromatous	Nonlepromatous	Normal	South Indian
I^{pp}	0.06880	0.07629	0.07572	0.06976
I^{pq}	−0.01444	−0.01808	−0.01676	−0.01633
I^{qq}	0.08819	0.09748	0.09180	0.09708

TABLE 9. *Variances in estimated gene frequencies in different populations.*

Variances	Type of population			
	Lepromatous	Nonlepromatous	Normal	South Indian
$V(_p)$	0.000088	0.000181	0.000063	0.000001
$V(_q)$	0.000113	0.000231	0.000076	0.000001
$V(_r)$	0.000164	0.000326	0.000111	0.000002

Indian population grouped by the King Institute of Preventive Medicine in Guindy, Madras.

2. Gene frequencies do not differ in the lepromatous population from gene frequencies in the normal and the South Indian populations.

3. No differences in gene frequencies are found when comparisons are made between the nonlepromatous population and the normal and South Indian populations.

4. No differences in the gene frequencies are found when comparisons are made between the lepromatous and nonlepromatous populations.

SUMMARY

On the basis of data now available with respect to ABO blood groups no significant difference is observed in the frequencies of the genes controlling the inheritance of the blood groups in the four types of populations considered in this study. The possibility, however, of revealing a relationship, if and when full blood grouping is carried out in families vis-a-vis other systems than ABO cannot be ruled out.

RESUMEN

Sobre base de los datos disponibles con relación a los grupos sanguíneos ABO, no se observa diferencia significativa de los genes que controlan la herencia de los grupos sanguíneos, en los cuatro grupos de población considerados en este estudio. Sin embargo, no debe descartarse la posibilidad de descubrir alguna relación siempre y cuando, se realize una tipificación completa de grupos sanguíneos en familias con respecto a sistemas distintos al ABO.

RÉSUMÉ

Sur la base des données se rapportant aux groupes sanguins ABO et qui sont actuellement disponibles, on n'observe pas de différence significative dans la fréquence des gènes qui contrôlent la transmission héréditaire des groupes sanguins, dans les quatre types de populations qui ont été étudiés. On ne peut toutefois exclure la possibilité d'une relation, qui pourrait être révélée par une étude éventuelle menée dans des familles et englobant une détermination complète des systèmes de groupes sanguins autres que ABO.

Acknowledgments. The authors are grateful to Major General P. N. Bardhan, the Director, for permitting us to publish this paper, to Mr. J. Swaminathan, Junior Scientific Officer, Division of Laboratories for doing the blood grouping, and to Mr. P. Sirumban, Statistical Assistant for his help in analysis of the data.

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