CHAPTER 3

GLYCOPHORIN-A (MN) ALLELIC DISTRIBUTION IN SOUTH INDIANS

3.1 ABSTRACT

Landsteiner and Levine discovered a blood group system in 1927 called the MN system and described three possible genotypes M, MN and N. The antigenic determinant of human MN system on erythrocytes is GPA. Studies on the distribution of blood groups of a population are one way to understand the population’s genetic makeup and susceptibility to disease. Blood samples were collected from 413 South Indian volunteers chosen randomly for the MN blood groupings. The gene frequencies were calculated using the gene counting method.

3.2. INTRODUCTION

Landsteiner and Levine described a blood group system in 1927 called the MN in which two alleles M and N determine the presence of corresponding antigens on red cells. According to this theory, three possible genotypes MM, MN and NN occur. GPA genes code for the determinant molecule for the MN blood groups in erythrocytes and are present on the 4q29 chromosome site. The GPA of human erythrocytes is a sialoglycoprotein with a chain of 151 amino acids and a molecular weight of 55,000 daltons. The M and N forms vary in their amino acid composition in positions 1 and 5 [1]. The M group has Serine and Glycine in positions 1 and 5.
respectively and the N group has Leucine and Glutamic acid in the respective positions as given below:

\[
A^N \quad \text{Leu-Ser}^* \text{-Thr}^* \text{-Thr}^* \text{-Glu}
\]
\[
A^M \quad \text{Ser-Ser}^* \text{-Thr}^* \text{-Thr}^* \text{-Gly}
\]

It was also suggested [2] that the two forms of the GPA evolved from a common ancestral gene by single base substitutions at the sites in the genome coding for aminoacids in positions 1 and 5 of the sequence.

The human GPA that spans the erythrocyte membrane in about \(5 \times 10^5\) copies per cell. The protein is present as two forms and three possible genotypes MM, NN or heterozygous MN can occur in a given population. These are inherited by means of two allelomorphic genes M and N at a single locus, but there is no dominance or recessiveness, so that while the cells of MM homozygotes are agglutinated by anti-M and those of NN homozygotes by anti-N, those of MN heterozygotes are agglutinated by both antisera.

Studies on the distribution frequencies of blood groups is one way to understand the population’s genetic makeup and susceptibility to disease apart from a host of other applications. Monospecific antibodies are required against the two GPA variant forms primarily to differentiate the three possible phenotypes (MM, NN and MN).

3.3. MATERIALS AND METHODS

Blood samples were collected from 413 South Indian volunteers who were chosen randomly for the MN blood groupings. Blood typing was done using commercial anti-M and anti-N antisera from Ortho Clinical Diagnostics, USA using standard
agglutination methods on glass slides. The results were recorded and the gene frequencies were calculated using gene counting method.

3.4. RESULTS

The results obtained from the present South Indian population study with respect to the distribution of MM, MN and NN blood groups are given in Table 1. The differences between the observed and the expected numbers of these blood groups are not statistically significant.

<table>
<thead>
<tr>
<th>Blood group</th>
<th>Number observed</th>
<th>Number expected</th>
<th>Allelic Frequency</th>
<th>$\chi^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>121</td>
<td>117.73</td>
<td>$M = 0.5339$</td>
<td></td>
</tr>
<tr>
<td>MN</td>
<td>199</td>
<td>205.55</td>
<td></td>
<td>0.4194</td>
</tr>
<tr>
<td>N</td>
<td>93</td>
<td>89.72</td>
<td>$N = 0.4661$</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>413</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Observed and expected numbers of the MN blood groups in the South Indian population along with the allelic frequencies and $\chi^2$ (H.-W.).

3.5. DISCUSSION

Since anti-M and anti-N antibodies occur only extremely rarely in human serum there is almost no danger of their causing trouble in blood transfusion. Thus they have been recognized as of little importance in medicine, and testing has largely
been left to geneticists. Thus data on the distribution of the MN blood groups have built up only very gradually over the years. The genetics of the system seem to imply that the N antigen is actually a precursor substance and the N gene is an amorph which leaves the N antigen unchanged while the M gene of the heterozygote converts part of the N antigen into M, and in the homozygote NN converts nearly all of the precursor to M. The MN antigens seem to have a direct interaction with membrane bound sialic acids, as M and N specificities seem to be linked to the presence of sialic acid variations. It has been suggested that the antigenic variations may result from specific sialyl transferase activities, which transfer sialic acids to disaccharides bearing specific T and Tn specificities that characterize specific cryptic antigens.

Of late, several associations with health conditions have surfaced with respect to the MN phenotypic expression in people. Most health problems are associated with the two "purebred" types (NN and MM), not with the mixed type (MN), a phenomenon known in genetics as hybrid vigor. It appears that the MN system may play a role in breast cancer. In general, persons with a family history of cancer are both type A and MM, it is probably advisable that he or she adopt an aggressive cancer-prevention lifestyle.

Possible association with the MN phenotypic expression to human health concerns comes from a number of studies. These include MN locus haplotypes with essential hypertension [3], [4], spinal osteochondrosis 1979, and also the effects of the MN blood group expression to serum LDL cholesterol level to a low fat diet [5].
An interesting application of the knowledge of the phenotypic expression of the MN system in humans comes from the usefulness of the GPA mutation assay, which is primarily a biodosimetric technique and is a reasonably good indicator of human health risk assessments. Mutational assays at the GPA locus developed till date use both the forms of monoclonal antibodies to detect the loss of the gene products from either of the two allelic forms [6]. Monoclonal antibodies facilitate the detection of mutant erythrocytes lacking either the N or the M products of the alleles among normal erythrocytes from the MN heterozygous individuals. The variant cell types, which can be detected, are those that lack the M form of the protein and those that lack the N form of the protein [7]. The erythrocytes are fixed and stained using monoclonal antibody- fluorochrome conjugates [8]. The erythrocytes are therefore doubly stained and the enumeration of the variant cells can be done by flow-cytometric analysis [9]. Although polyclonal typing sera are commercially available, monoclonal antibodies for the two forms of the human GPA became a necessity for the GPA mutation assay as initially developed, which employs flowcytometric studies.
REFERENCES


