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Discovery of human blood groups in India

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Review Article

Discovery of human blood groups in India

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Abstract

Over 300 blood group antigens have been discovered in different parts of the world and most them are classified into 35 systems. India has contributed a few rare blood groups including the Bombay phenotype, Indian blood group antigens like In(a), In5 and I-i- phenotype. Besides, there are a few other rare blood groups, though not discovered in India, were encountered here including a host of the weaker variants of A, B and H antigens, the ultra-rare Mg antigen of the MNS blood groups, phenotypes like D- -, Rh-null, I-int, In(b-), Colton-null and r(y).

Key words: Blood group phenotypes, Bombay blood group, In(a), In5, Mg, I-i- phenotypes

Over 300 human blood group antigens have been recognized and classified into 35 systems. Each system has its own antigen make-up. Many of these antigens were discovered over a period in different parts of the World, mainly in the West. Steve Pierce and Marion Reid has compiled a historical account and lucidly presented it in form of a book.[1] India has also made its contribution in the field of blood groups with a few of the original discoveries as outlined here.

"Bombay" phenotype

The "Bombay" blood group was discovered in December 1951. A patient, who had met with a railway accident, was grouped as O but none of the 115 group O donors were found matching due to the presence of a particular antibody. The following month, another patient with stab-wound injury, presented compatibility problem with group O donors. However, both these patients were mutually compatible. Later, a deliberate search yielded one more donor with identical characteristics. These blood samples were referred to BGRU, London for further work up, where it was declared to be a "new" blood group[2] and was later named as "Bombay" phenotype. While ordinary group O persons have a high frequency antigen (HFA) H present on their RBCs, individuals with "Bombay" phenotype lack H antigen on their RBCs, hence the phenotype is also denoted as Oh. A person with Oh phenotype has naturally occurring anti-H akin to antibodies of the ABO blood groups.

In a systematic search, 3 out of 42,297 samples screened were found to be Oh phenotype suggesting to its frequency as 1:13000 in the general population in Mumbai.[3] Further screening, based on increased sample size from two major hospitals, viz., KEM and J J hospitals in Mumbai, overall incidence was improved to 1:7600 with 22 cases among the 1,67,404 samples screened. Half of the cases belonged to the south-west of Maharashtra, in particular to the regions of Konkan and Goa.[4] In view of this, in a survey made in 400 villages from this region, an incidence of Oh phenotype in this region was worked out to be 1:4000 (six cases among 24,085 individuals screened)[5] that gained support from previous observation. The cases were referred from most states of India in varied numbers but the majority was from western and southern Indian states. By the year 1988, a total of 179 cases were recorded with state-wise distribution as Maharashtra (122), Karnataka (15), AP (8), Goa (6), Gujarat (5) to name a few.[6]

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The discovery of the "Bombay" phenotype had well explained the basics of the biosynthesis of the ABO blood group antigens.

I-i- Phenotype

The I blood group system is characterized as a developmental antigen, i.e., I antigen is weakly expressed on the fetal RBCs and gradually strengthen over a period of 18 months to reach a peak to remain stable through the adult life. An antigen showing a reciprocal character to I was termed as i, and is strongly expressed on the RBCs from newborns and weakens gradually through this period and remains weak in adult life.[7] Some rare adults with the I-i antigens strength similar to that of the newborns are under genetic influence and considered homozygote for the I negative status so were termed as adult-ii, the heterozygote members in the family shows an intermediate reaction pattern for the Ii antigens and are classified as I-int.

We had encountered healthy blood donors with depressed I antigen on RBCs to the level of newborns without any concomitant rise of the i antigen. We termed this phenotype as I-i-.[8] It was found with a frequency of 1:900. The family study among the three propositi showed no other members having this phenotype. However, in a larger family, three more members with I-i- phenotype were noticed. One family, with 95 members, had as many as 15 I-i- members and six others with a partial suppression of the I antigen.[9] While the phenotype was found to be familial in character, its inheritance did not apparently follow the Mendelian law of inheritance presumably due to the complexity in interaction of the other blood groups including the ABH at biosynthetic level. Interestingly, all the individuals with this phenotype belonged to A1 or A1B and the A1 antigen strength on their RBCs was significantly higher when compared to those with normal complements of I-i antigens thereby suggesting the association between the ABO and the I blood groups at precursor level.

Indian antigens

In^a

In the year 1970, an immune serum with anti-Rh.D was referred by the diagnostic firm for QC. Although, the serum showed a presence of potent anti-D, it reacted with certain D-neg RBCs as well. An additional antibody, isolated by absorption-elution methods, was found to be reacting with the RBCs of about 2-3% of the random blood samples. After preliminary work up, the same absorbed serum was referred to the Blood Group Reference Laboratory, London for further investigations. Initial reports showed no reactivity against the panel of red cells tested. Second consignment, of the serum along with the reacting red cells, was sent for reinvestigation. Then it was reported that the serum did have reactivity against the antigen on red cells that was provided but the same was absent on their red cell panel. The antibody was confirmed as a hitherto unknown antigen and was named after India, and being the first of its kind, was termed as In(a).[10]

The significance of this discovery was soon realized when about 30 commercial anti-D reagents produced in India were tested and found to have anti-In(a). The reason for this was that several Rh.D-(Rh subtype rr, cde/cde) voluntary paid donors (VPDs) were immunized for the production of anti-D using RBCs of one VPD named *IS* (Rh subtype R_or, cDe/cde) who incidentally possessed the antigen to be discovered later as In^a. While such anti-D reagents were in use, about 3-5% of the Rh.D- bloods might have been falsely entered as Rh.D+.

Discovery of In(a) paved way to identify its antithetical antibody, called Salis, to a high frequency antigen (HFA) detected earlier. The Salis antibody was rechristened as anti-In(b).[11] The Indian system was expanded when two other antigens, INFI (In3) and INJA (In4) were recognized in the year 2007.[12]

In5 (INRA)

The Indian blood group system was further expanded when an antibody to an HFA was found during the routine pre-transfusion compatibility tests. Preliminary investigations indicated to its specificity within the Indian system, though its specificity to In(b) as an HFA was ruled out as the RBCs reacted with two examples of anti-In(b). The blood specimen was referred to IBGRL, Bristol, UK to rule-out or rule-in the specificity to the other two

known HFA of the Indian system, viz., In3 and In4. The patient's RBCs were typed positive for In3 and In4 thus ruling out these specificities. The RBCs were typed positive for the host of HFAs like Kn^a, McC^a, Yt^a, U, Vel, En^a, Kp^b, Js^b, Wr^b, Ge and CD99 excluding its specificities to these antigens. The patient's antibody reacted with RBCs of rare bloods like In(b-), In:-3, In:-4, $Gerbich_{null}$, Rh_{null}, D- -/D- -, M^kM^k, Fy(a-b-), Gy(a-), and $K_{0,}$ further ruling out its specificity to these antigens. The findings indicated to its serological specificity against a hitherto unknown antigen.

A striking observation was its weak reactivity with the RBCs from Lu(a-b-(InLu). CD44 (IN) antigens were known for their suppression on RBCs from Lu(a-b-(InLu) phenotype.[13] Hence, the molecular typing on exons of the haemopoeitic isoform of the CD44 (*IN*) gene was ensued. The result showed a novel homozygous missense mutation c.449G>A in exon 5 of *CD44* encoding p.Arg150His amino acid substitution at the protein level that explained the lack of a novel HFA.[14] We coined its name as INRA, taking the first two letters from the name of the blood group system and the last two letters from the patient's name as per convention. ISBT recognized the INRA as a new antigen of Indian blood groups and assigned the numerical term as In5.

Other novel features found in the Indian Population

Apart from these, India has discovered the anti-H Kantola lectin *Momardica dioica* in an Indian plant,[15] Citrate dependent anti-H,[16] Streptomycin antibiotic dependent panagglutination,[17] Bicarbonate anion dependent ant-"N",[18] and spontaneous cold agglytination (SpCA) phenomenon.[19] Besides, there are also several rare phenotypes, though not discovered in India, have their presence in India. These include a host of the weaker variant of A, B, and H antigens,[20] ultra-rare Mg antigen of the MNS blood groups,[21] phenotypes like D- -,[22] Rh-null,[23] I-int,[24] In(b-),[25] Colton-null[26] and r(y).[27]

Conclusion

India has contributed towards the discoveries of a few blood groups including the Bombay phenotype, Indian blood groups, i.e., In(a), In5 and the I-i- phenotype. Besides, there are a few other rare blood groups, though not discovered in India, have been encountered here including a host of the weaker variants of A, B and H antigens, ultra-rare Mg antigen, phenotypes like D- -, Rh-null, I-int, In(b-), Colton-null and r(y). Of these, six phenotypes are of transfusion significance, viz., Bombay (Oh), D- -, Rh-null, In(b-),In5 and Colton-null. The supply of these rare bloods for transfusion could be a challenging task for the recipients who have developed alloantibodies through transfusion and/or pregnancies.

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