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RESEARCH ARTICLE

QUALITY PERFORMANCE OF BLOOD GROUPING REAGENTS IN LAST FIFTEEN YEARS: INDIA

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ABSTRACT

Quality control (QC) is a critical component of Laboratory Quality Management System for reliability of testing results.1Batch release by manufacturer of blood Grouping Reagents is mandatoryonly after products QC performance. The laboratory has evaluated a total number of 1320batches of different Blood Grouping Reagents types by haemagglutination technique. Out of 1320 batches, 275 were indigenous manufacturers and 1045 were imported. 242 of 275 indigenous batches were recommended and 33 were not recommend. 1003 of 1045 imported batches were recommended and 42 were not recommended. 94.3% of total 1320 batches were recommended and 5.7% were not recommended. The most serious risk is an acute haemolytic transfusion reaction caused by blood type-incompatible transfusion. Blood type-incompatible transfusion is one of the leading causes of transfusion-related deaths. The incidence of ABO-incompatible transfusion is estimated to be 1:38,000 to 1:100,000 units of RBCs in the United States, 1:16,500 to 1:100,000 units of RBCs in the United Kingdom, and around 1:100,000 units of RBCs in Canada.1Laboratory diagnostic services play a critical role in all health-related decisions both of an individual as well as of the population.

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INTRODUCTION

Discovery of the ABO blood group system by Landsteiner in 1901 laid the foundation of immunohematology, blood transfusion and transplant biology. Development of anticoagulant preservative solutions made it possible to store blood and hence separate the blood donation process from the recipient transfusion and establish "blood banks." The first blood bank in the world was set up in Madrid in 1936, during Spanish Civil War. In India, the first blood bank was established in Kolkata in 1942 at the All India Institute of Hygiene and Public Health to meet war needs. It was later shifted to Kolkata Medical College in 1945, where it started functioning as the first civilian blood bank in the country. (Neelam Marwaha, 2014) India currently has over 11,500 hospitals, 14,000 diagnostic laboratories[3]and 2545 authorized Blood banks**.** (Jaspreet Kaur Boparai and Surjit Singh, 2015) In 1950, Levey and Jennings introduced the statistical control theory of industrial product manufacturing into the clinical laboratory and established the initial clinical examination analysis quality control (QC)**).** (Yang Yu *et al*., 2013)

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Commercial antibodies are extensively used in research, diagnostic and therapeutical applications. While diagnostic and therapeutical antibodies are subject to stringent regulations by health authorities throughout the world, there are no standards or third-party quality controls for research antibodies. Lotto lot variation exists in terms of specificity and performance. Reseachers have recognized this important quality issue. (Mary Johnson *et al*., 2015) A good understanding of country's laboratory services is needed for success in the programs related to health and laboratory. In case of India, diverse types of laboratories are present, which are either public or private sector diagnostic laboratories, which can be further classified into 'Hospital-attached' laboratory (HAL) and 'Stand-alone' laboratory (SAL). HALs are either present within the hospital ('Hospital-attached fixed' laboratory (HAFL)) or attached to the hospital ('Hospital-attached mobile' laboratory (HAML)). SALs are laboratories not attached to hospitals, run by government, individuals or corporate. (Rahi Jain and Bakul Rao, 2015) National blood policy and organization Providing safe and adequate blood should be an integral part of every country's national health care policy and infrastructure. Other than QC of blood grouping reagents, haemovigilance also play an important role in transfusion safety. (Newsletter, 2015).

Table 1. Results of 1320 batches QC Samples

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Sl. No.1	Type of QC sample	Total QC Sample					Indigenous QC Sample					Imported QC Sample		
		T	R	R (%)	NR	NR (%)	R (IND)	R (IND) %	NR (IND)	NR (IND) %	R (IMP)	R (IMP) %	NR (IMP)	NR (IMP) %
2	Anti-A	280	269	96	11	4	50	83.3	10	16.7	219	99.54	1	0.45
3	Anti-B	231	222	96.1	9	3.9	44	89.8	5	10.2	178	97.8	4	2.2
4	Anti-AB	130	124	95.3	6	4.7	36	100	0	0	88	93.6	6	6.4
5	Anti-D (IgM)	161	155	96.3	6	3.7	31	86.1	5	13.9	124	99.2	1	0.8
6	Anti-D (Blend)	157	156	99.3	1	0.7	26	100	0	0	130	99.2	1	0.8
7	Anti-D (IgG)	23	23	100	0	0	9	100	0	0	14	100	0	0
8	Anti-H (Lectin)	18	15	83.3	3	16.7	3	100	0	0	12	80	3	20
9	Anti-A1 (Lectin)	27	15	55.6	12	44.4	4	44.5	5	55.5	11	61.1	7	38.9
10	AHG	61	49	80.3	12	19.7	5	38.5	8	61.5	44	91.6	4	8.4
11	Grouping Cards	232	217	93.5	15	6.5	34	100	0	0	183	92.4	15	7.6
12	Total=	1320	1245	94.3	75	5.7	242	88	33	12	1003	96	42	4

T- Total, R- Recommended, NR- Not Recommended, IND- Indigenous, IMP- Imported.

Market Overview

The Indian diagnostic market comprising primarily of reagents and kits is to a large extent import driven. Reagents and kits will also be major contributors to growth. There is increasing need for indigenous products with affordable prices.

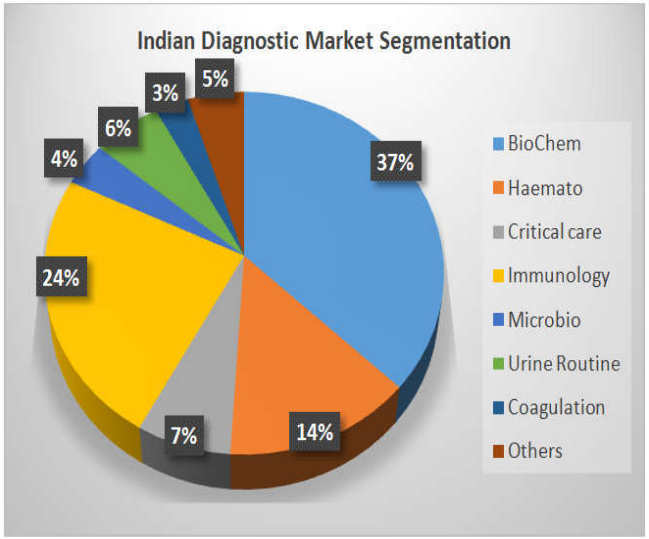


Fig. 1.

Today the total Indian healthcare sector, which is currently valued at $34 billion, is projected to grow to nearly $40 billion. The diagnostic and pathology market is around 2 percent of the overall healthcare market. The diagnostic market has been growing at 15-20 percent and by all indications shall continue to grow for another 10 years at this rate. In Vitro-Diagnostic (IVD) Market accounts for about 38 percent of the total global medical devices and diagnostic market. In a very short time, India is poised to catch up with the global IVD market. Current use of Blood Grouping reagents in India: Consumption trends-Steady, Type of Testing – Haemagglutination, Compounded Annual growth Rate (2004-08)-5.7%, Major Consumers- Clinical Labs and Hospitals. (FINPRO, 2008)

Regulations

IVD market is highly regulated. Diagnostic kits and reagents belong to the category of drugs; Critical diagnostics products are regulated under Drugs and Cosmetic Rules 1945, and must be registered before they can be sold in India. They also require an import license. As in case of manufacturing, Central Drugs Standard Control Organization (CDSCO) functioning Directorate General of Health Services (DGHS) is led by Drug Controller General of India (DCG (I) is the leading organization responsible for quality control of imported diagnostics products.

It is also the licensing authority for the approval of new products proposed to be imported. All the diagnostics products to be manufactured or sold in India require license. For licensing purposes the IVD devices have been divided into two groups: critical and non- critical devices. Critical devices include the ones used for: HIV, HBs Ag, HCV, Blood grouping reagents and Malaria tests. All others are considered non-critical. (FINPRO, 2008)

MATERIALS AND METHODS

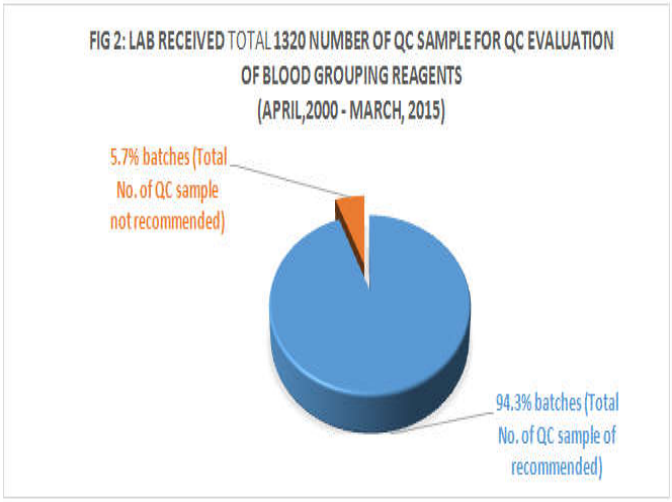
Lab received 1320 batches of9 different type products for Blood Grouping Reagents (Anti-A, Anti-B, Anti-AB, Anti-D (IgM),Anti-D (IgG+IgM) Blend, Anti-D (IgG), Anti-H (Lectin), Anti-A1 (Lectin), Anti-Human Globulin (AHG) and Blood grouping cards, Blood group antigens are tested through haemagglutination techniques, the tube technique being the gold standard for over a century. High throughput and multiple antigen/antibody testing platforms are available.[2]Blood Grouping Reagents are tested for their Physical Appearance, Potency, Avidity, Intensity, Specificity, Rouleaux, Haemolysis and Prozone, IgG/C3d parameters as per regulatory guidelines and have values greater than or equal to the appropriate International Standards or suitable reference preparation used.[10]Blood Reagent Laboratory at National Institute of Biologicals, Noida (India) is the only Central Drugs Laboratory for in-vitro Blood Grouping Reagents and has been evaluating the reagents forwarded by DCG(I). (Guidance Manual)

RESULTS

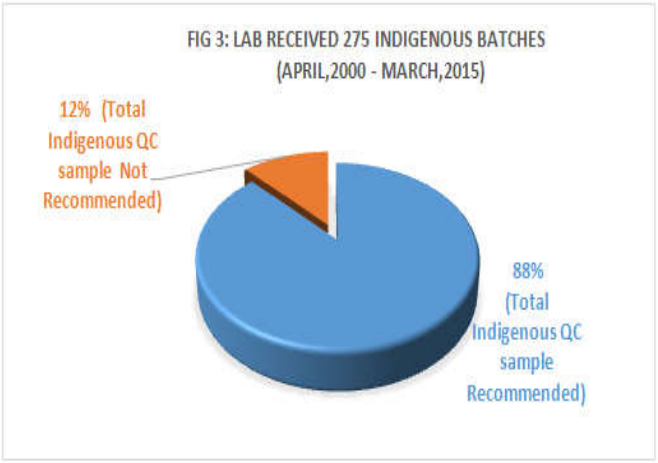
In last fifteen year (April,2000- March,2015) the laboratory received 1320batches of 9 different type of Blood Grouping Reagents of Anti-A, Anti-B, Anti-AB, Anti-D (IgM),Anti-D(IgG+IgM)Blend, Anti-D (IgG), Anti-H (Lectin), Anti-A1 (Lectin), Anti-Human Globulin (AHG) for Coombs test, major/routine and Gel Card technique, Microplate system and Blood Grouping Cards for QC evaluation and batch release certification.[11]The laboratory has evaluated a total number of 1320 batches of different type Blood Grouping Reagents by haemagglutination. Out of 1320 batches, 275 of were indigenous manufacturers and 1045 were imported. 242 of 275 indigenous batches were recommended and 33 were Not recommend. 1003 of 1045 imported batches were recommended and 42 were not recommended. 94.3% of 1320 batches were recommended and 5.7% were not recommended. Table No.-1 Shows the details results of QC evaluation of blood grouping reagents. The laboratory has evaluated a total number of 1320 batches of different type Blood Grouping Reagents by haemagglutination. Out of 1320 batches, 1245 were recommended and 75 were not recommended (Fig: 2).

DISCUSSION AND CONCLUSION

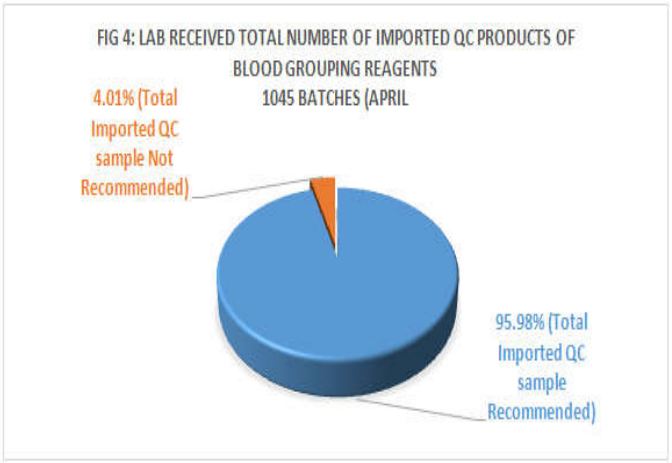
QC of Blood Grouping Reagents is essential for blood group screening of donors and recipients. The laboratory has evaluated a total number of 280 batches of Anti-A. Out of 280 batches, 60were indigenous manufacturers and 220 were imported. 50 (83.3%) of 60 indigenous batches were recommended and 10(16.7%) were Not recommended. 219



The laboratory has received a total number of 1320 batches, out of which 275 batches were indigenous. Out of 275 batch, 242 were recommended and 33 were not recommended (Fig:3).

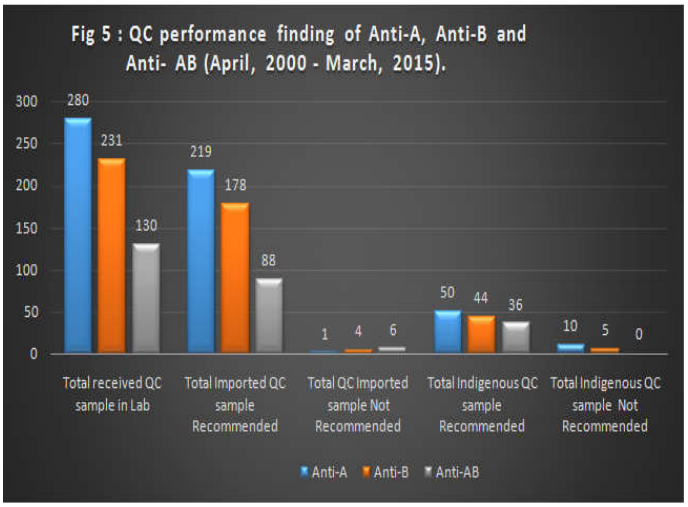


The laboratory has received a total number of1045 imported batches, out of which 1003 batches were recommended and 42 were not recommended (Fig:4).

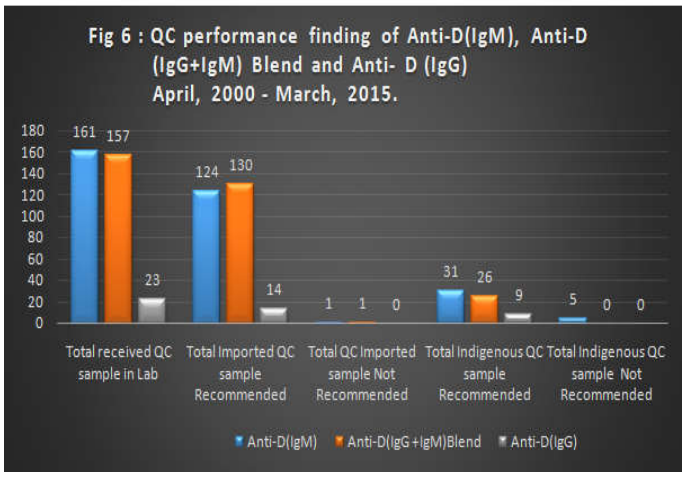


(99.54%) of 220 imported batches were recommended and 1(0.45%) were not recommended. Total number of 231 batches of Anti-B received, Out of 231 batches, 49 were indigenous

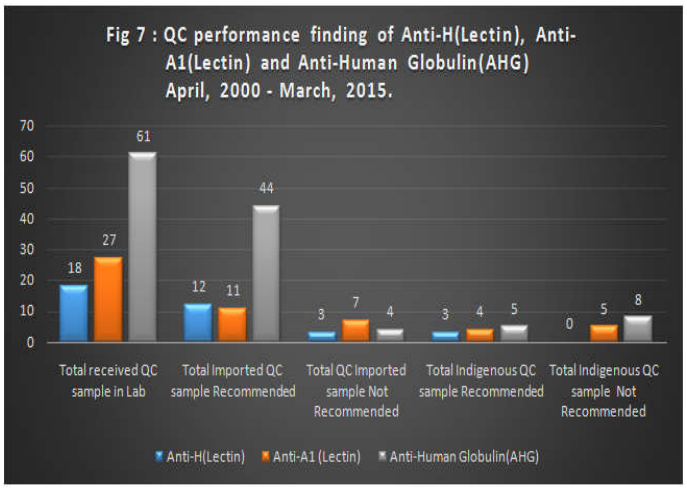
manufacturers and 182 were imported. 44 (89.8%) of 49 indigenous batches were recommended and 5 (10.2%) were Not recommended. 178 (97.8%) of 182 imported batches were recommended and 4 (2.2%) were not recommended. Total number of 130 batches of Anti-AB received, Out of 130 batches, 36 were indigenous manufacturers and 94 were imported. 36 (100%) of 36 indigenous batches were recommended and 0 (100%) were not recommended. 88 (93.6%) of 94 imported batches were recommended and 6 (6.4%) were not recommended (Fig: 5).



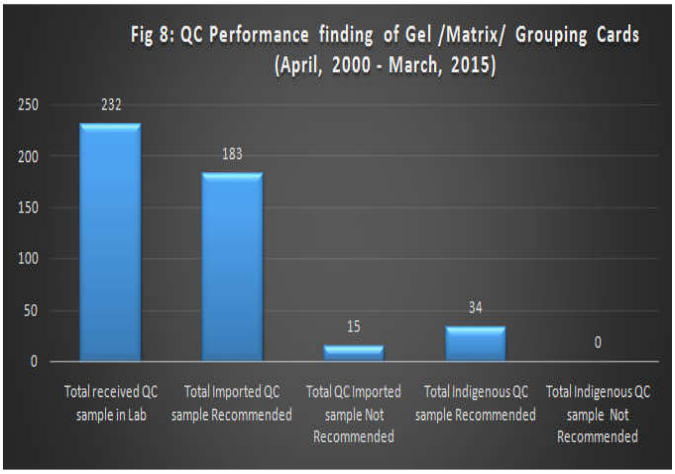
Total number of 161 batches of Anti-D (IgM). Out of 161 batches, 36 were indigenous manufacturers and 125 were imported. 31 (86.1%) of 36 indigenous batches were recommended and 5 (13.9) were Not recommended. 124 (99.2%) of 125 imported batches were recommended and 1(0.85%) were not recommended. Total number of 157 batches of Anti-D (IgG+IgM) Blend received, Out of 157 batches, 26were indigenous and 131 were imported. 26 (100%) of 26 indigenous batches were recommended and 0 (100%) were Not recommended. 130 (99.2%) of 131 imported batches were recommended and 1 (0.8%) were not recommended. Total number of 23 batches of Anti-D (IgG) received, Out of batches, 9 were indigenous and 14 were imported. 9 (100%) of 9 indigenous batches were recommended and 0 (100%) were Not recommended. 14 (100%) of 14 imported batches were recommended and 0 (100%) were not recommended (Fig: 6).



18 batches of Anti-H (Lectin). Out of 18 batches, 3 were indigenous manufacturers and 15 were imported. 3 (100%) of 3 indigenous batches were recommended and 0 (100%) were Not recommend. 12(80%) of 15 imported batches were recommended and 3(20%) were not recommended. Total number of 27 batches of Anti-A1 (Lectin) received, Out of 27 batches, 9were indigenous and 18 were imported. 4 (44.5%) of 9 indigenous batches were recommended and 0 (100%) were Not recommended. 130 (99.2%) of 131 imported batches were recommended and 5 (55.5%) were not recommended. Total number of 61 batches of Anti-Human Globulin (AHG) received, Out of 61batches, 13 were indigenousand 48 were imported. 5 (38.5%) of 13 indigenous batches were recommended and 8 (61.5%) were Not recommended. 44 (91.6%) of 48 imported batches were recommended and 4 (8.4%) were not recommended (Fig :7).



The laboratory has evaluated a total number of 232 batches of Gel/Matrix or Grouping cards. Out of 232 batches, 34 were indigenousand 198 were imported. 34 (100%) of 34 indigenous batches were recommended and 0 (100%) were Not recommended. 183 (92.4%) of 198 imported batches were recommended and 15 (7.6%) were not recommended. (Fig :8).



The most serious risk is an acute hemolytic transfusion reaction caused by blood type-incompatible transfusion. According to a recent report by the United States Food and Drug Administration (US-FDA), ABO-incompatible transfusions

account for 10% of all transfusion-related deaths. Most blood type-incompatible transfusions result from human errors with 10% of these arising through incorrect medical prescriptions, 40% in blood banks, and 50% in pre-transfusion compatibility testing (Gui-Ping *et al*., 2015). Most clinical pathology laboratories purchase their in vitro diagnostic reagents, calibrators and quality control materials from a variety of national and international in vitro medical diagnostic devices manufacturers. (In vitro) It is essential that blood grouping reagents are prepared using reliable manufacturing procedures that are consistently capable of producing safe and efficacious products. The products must comply with requirements of respective international standards. (International Society of Blood Transfusion, 1984) The standard of work performed in any laboratory is determined by the expertise of the staff, the availability of equipment and apparatus, and the quality of reagents used. Without high quality reagents the ability of the staff to perform work of high standard is compromised. Probably in no other area of laboratory medicine does the consequence of a mistake have so great a potential danger to the patient as in the blood bank. There is no way in which a clinician can evaluate the accuracy of a blood group report and in this area clinical judgments counts for nothing. It follows that blood group studies, although simple in principle, are heavy in responsibility. Every precaution to ensure accuracy of results must be taken, and a quality assurance program, designed to confirm the effectiveness of reagents before they are used, is an important aspect. Correct handling and storage of reagents is a part of quality assurance (Marsh).

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