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Marching TowardsChemiluminescence Immunoassaysin Screening of Donors for Blood Borne Viral Infections

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Abstract:*The Chemiluminescence Immunoassays (CLIA) and Enzyme linked ImmunosorbentAssays (ELISA) per se are widely used diagnostic tools for detection of specific antigens and / or antibodies present in the sample of interest. The ELISA is a most common and straightforward technique, which involves a number of variables, such as reagent / sample addition, microtiter plate washing, incubation temperature and time etc., hence, if, the test is not performed correctly it can affect subsequent steps and finally the end results also. Whereas, now a days CLIA is quick,* simple, human error free as it performs complete automatic sample processing, testing*and provides clear interpretation of the test results.*
The present small study reveals the shift in India towards CLIA from ELISA for screening of HIV-Ab,HBsAg, and HCV-Ab due to better sensitivity and swift testing of CLIA which is evident from four years data viz. 2012 to 2016. The number of batches of both types of immunoassays received during this period clearly shows a substantial increase in CLIA testing comparing to the ELISA. It is concluded that CLIAis well established as one of the better alternative methods of conventional or traditional ELISA for detection of antigen and / or antibodies of the blood borne viral infections including Human Immunodeficiency Virus, Hepatitis C Virus and *Hepatitis B Virus.*

Key World: *Immunodiagnostic Kit, Chemiluminescence Immunoassay, Enzyme Linked Immunosorbent Assay, Human Immunodeficiency Virus, Hepatitis B Virus,Hepatitis C Virus*

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I. Introduction

Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV) and Hepatitis B Virus (HBV) are responsible for Transfusion Transmissible Viral Infections. Hence, transfer of safe blood, blood components or blood products from one donor to recipient requires proper screening of blood for HIV, HCV &HBV infections. Historically, blood donor screening was using health histories, a self-deferral process and pre-selected donor groups to enhance blood safety. The numbers of transfusion-transmitted infectious diseases (TTIDs) were rather increased in the beginning of the late 1930s [1]. Since then there has been significant development in blood transfusion services.

According to the World Health Organization (WHO) all donated blood need to be tested for HIV, HBV, HCV, Treponema pallidum (Syphilis) and even as per Drugs & Cosmetic Acts & Rules, 1945 Govt. of India, the donated blood should be free from Hepatitis B surface antigen , HCV antibodies, HIV I and HIV II antibodies, syphilis and malarial parasite [2].

These blood-borne viruses are transmitted through contaminated blood transfusion, parenteral route, contaminated syringes, unprotected sexual intercourse, contaminated surgical equipment or other sharp instruments etc. Not only do they establish asymptomatic persistent infections with occasional sequelae, but they also cause significant morbidity and mortality when transmitted through transfusion of blood and blood products [3].

The screening of these viral infections is performed by immunoassay, an important strategy for the safe transfusion, prevention and cure for public health.Presently, different kinds of screening assays / immunoassays are commercially available in the Indian marketvizRapid, ELISA, CLIA &Enzyme Linked Fluorescence Assay (ELFA) [4]. The ELISA was developed in year 1971 and it enhanced the performance of immunoassay for diagnosis of infectious diseases. It is a kind of immunoassay that uses enzyme labelled antibody/antigen to detect antigen/antibody, and is well known in the bio-analytical field [5, 6]. Immunoassays became simpler to perform and popular when techniques to link enzymes to antibodies were developed in the late 1960s [5]. Over

all ELISA test is a better diagnostic tool as compared to the Rapid test but it has some limitations like the indefinite enzyme-mediated colour change and others. Over a sufficiently long period of time, the colour strength inaccurately reflects the higher amount of primary antibody present, yielding false-positive results. Nonspecific binding of the antibody or antigen to the plate leads to a falsely high-positive result [7]. However, the need to detect increasingly smaller amounts of target molecules has led to the emergence of more sensitive test methods such as fluorescence or chemiluminescence based tests.

Chemiluminescence is a technique in which the antigen or antibody is labelled with a molecule capable of emitting light during a chemical reaction; this light is used to measure the formation of the antigen-antibody complex [8]. This immunoassay is a variation of the standard ELISA. As this assay was reported in 1985 by Woodhead [9], it has been applied widely to the clinical diagnosis and environmental analysis [10]. This technique has also been used as a diagnostic tool in medical sciences and also used in various fields like environmental monitoring, food safety, pharmaceutical analysis and bacterial identification[11].In the preliminary stage, CLIA used luminol, isoluminol, acridinium ester and so on directly labelling antigen or antibody [10,12,13] Therefore, the present paper deals about comparative use of CLIA and ELISA as well as to see its superiority in screening of blood samples for testing of these three blood borne viral infections.

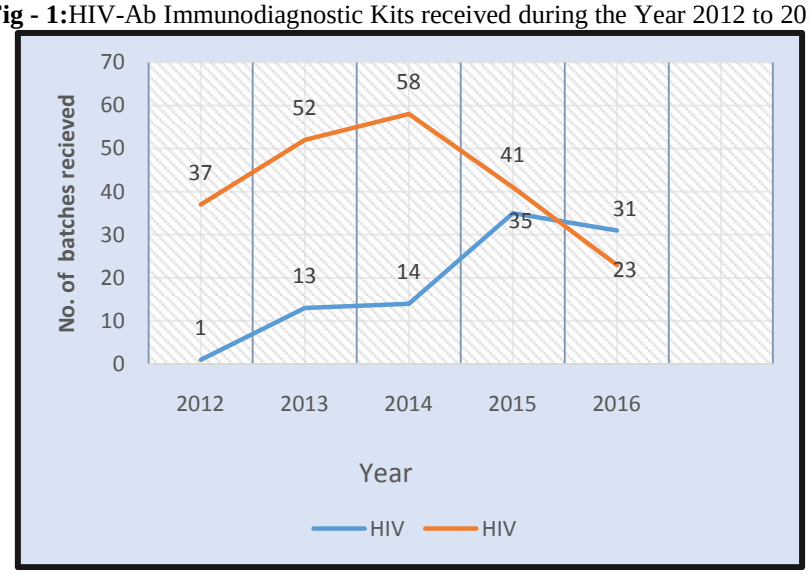
II. Materials And Methods

The collected data was analysed for the ELISA and CLIA batches of HIV-Ab, HCV-Ab and HBsAg received from January, 2012 to December, 2016. During this period a total number of 1041batches were received at National Institute of Biologicals (NIB), NOIDA which were forwarded by the Offices of Central Drugs Standard Control Organization, Food and Drugs Administration, New Delhi, INDIA. The ELISA and CLIA based diagnostic kits used for detection of HIV-Ab, HCV-Ab and HBsAg were taken into account for the present study.

III. Results

In case of HIV-Abimmunodiagnostic kits during the year 2012, only one batch of CLIA based kit was received, whereas, 37 batches of ELISA based kits were received for Quality Control Testing. Gradually, there was increase in batches of CLIA kits viz. 13, 14, 35, 31 in the year 2013, 2014, 2015 and 2016 respectively and 37, 52, 58, 41 and 23 batches of ELISA kits in the year 2013, 2014, 2015 and 2016 respectively (Fig – 1). During these five years rise in the number of batches of CLIA based kits was observed for HIV-Ab, HCV-Aband HBsAg. In the year 2016 higher number of batches of CLIA based kits of HIV-Ab, HCV-Aband HBsAgwere received as compared to ELISA.

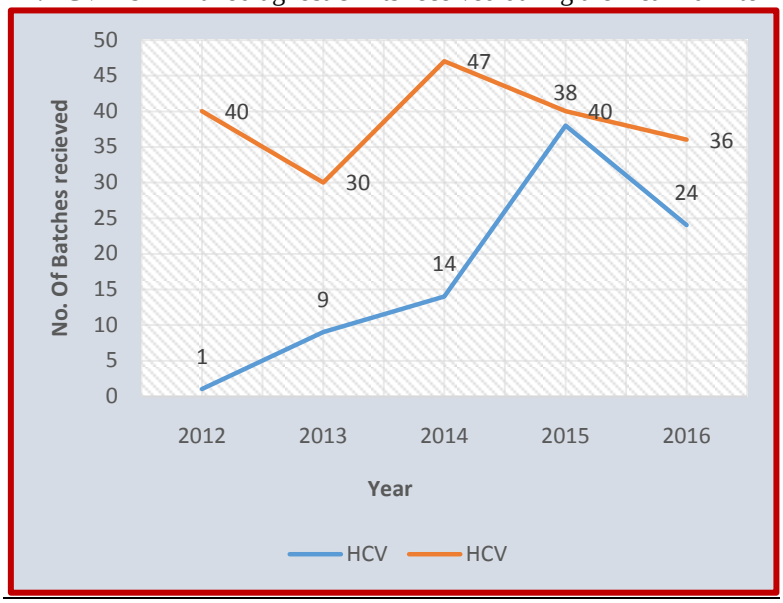
Fig - 1:HIV-Ab Immunodiagnostic Kits received during the Year 2012 to 2016



Similarly, in the year 2012 a total number of 41 batches of HCV-Ab immunodiagnostic kits were received. Out of which only 1 batch was based on CLIA and 40 batches were based on ELISA. In the year 2013, 2014, 2015 & 2016 the number of batches of CLIA based kits received were 9, 14, 38 and 24 respectively. The number of batches of ELISA based kits received in the year 2013, 2014, 2015 & 2016 were 30, 47, 40 and 36

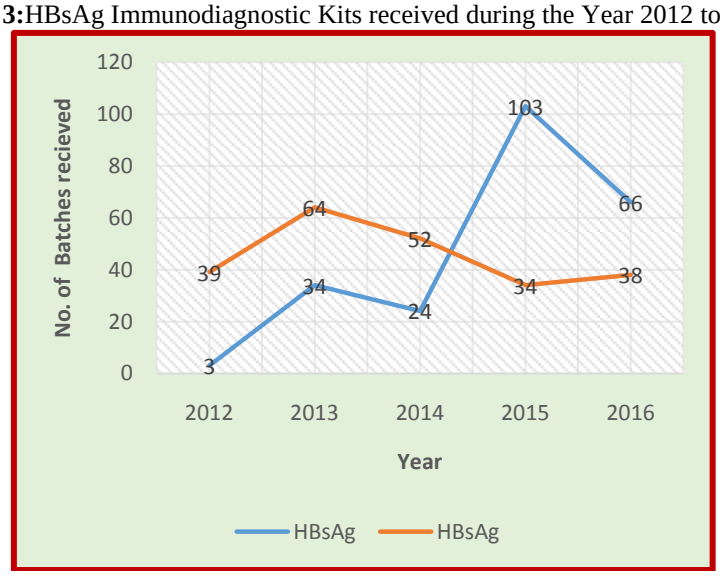
respectively (Fig – 2). In year 2015, there was approximately 50% increase in CLIA based kits as compared to ELISA kits received in year 2014.

Fig - 2:HCV-Ab Immunodiagnostic Kits received during the Year 2012 to 2016



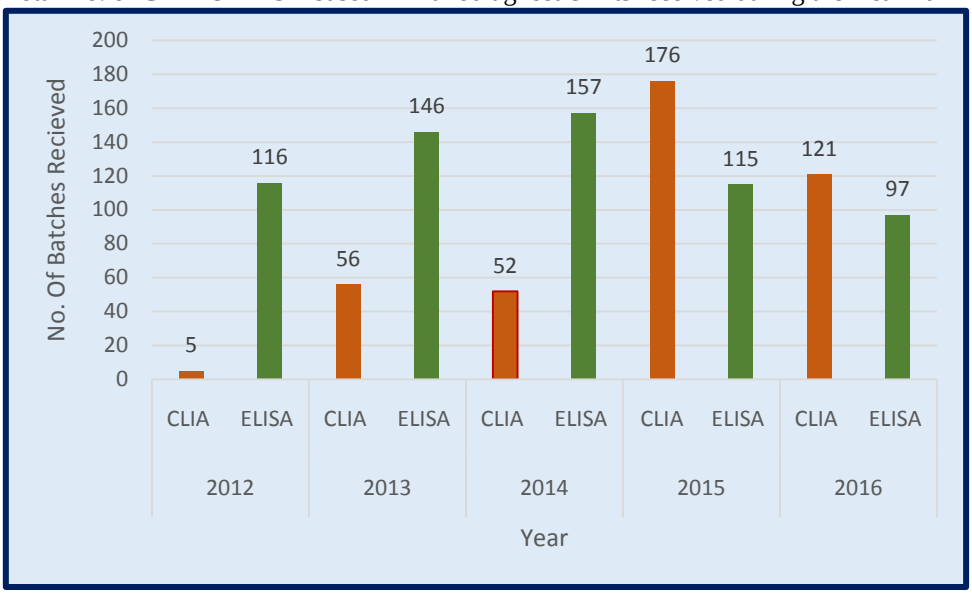
A total of 42 batches of HBsAg immunodiagnostic kits were received during the year 2012.Out of which 39 were based on ELISA and 3 were based on CLIA. The number of batches of CLIA kits increased to 34, 24, 103 and 66 during the year 2013, 2014, 2015 & 2016 respectively. Whereas the number of batches of HBsAg ELISA kits received in the year 2013, 2014, 2015 & 2016 were 64, 52, 34 & 38 respectively. A significant increase in the number of batches of CLIA kits was observed during these five years particularly in the year 2015 (Fig-3). In this year the laboratory has received 103 batches of CLIA based HBsAg kit as compared with 34 batches of ELISA based kits. In the year 2016, 57% increase was observed for CLIA as compared to ELISA.

Fig - 3:HBsAg Immunodiagnostic Kits received during the Year 2012 to 2016



In the year 2012, a total number of 121 batches for HIV-Ab, HBsAg and HCV-Ab were received. Out of which 05 batches of CLIA based and 116 batches of ELISA based immunodiagnostic kits were received. In year 2013, 2014, 2015 and 2016 the total number of batches of HIV-Ab, HBsAg and HCV-Ab received were 56, 52,176 and 121 respectively and for ELISA the total number of batches of HIV-Ab, HBsAg and HCV-Ab received were 146, 157, 115 and 97 for year 2013, 2014, 2015 and 2016 respectively (Fig – 4). In year 2015 and 2016 a sizeable increase in CLIA based immunodiagnostic kits has been observed as compared to ELISA immunodiagnostic kits received for Quality Control Testing.

Fig - 4: Total No. of CLIA &ELISA based Immunodiagnostic Kits received during the Year 2012 to 2016



IV. Discussion

Innovation and / or improvement of different categories of immunodiagnostic kits are an on-going exercise for better and early diagnosis of any disease. Whenever, such kind of approaches are seen in In-vitro Medical Devices (IVDs), then a variety of immunoassay products are being dramatically developed for diagnosis of fatal diseases like Human Immunodeficiency Virus, Hepatitis Cand Hepatitis B.CLIA is a wonderful example of these kind of approaches. It is a High Throughput Screening (HTS) platform for diagnosis of a lot of infectious diseases. This technique has been in use as diagnostic tools in medical sciences and also in various fields like environmental monitoring, food safety, pharmaceutical analysis and bacterial identification [11]. Now a day's CLIA is well established as one of the alternative methods of conventional or traditional ELISA for detection of blood borne viral infections. The trend towards inclination for CLIA based immunodiagnostic kits may be because of beingclosed system and requires less human intervention,therefore, the chances of error are reduced while in case of ELISAall steps are manual and hence increase the chances of error. In addition CLIAtechnology is highly sensitive, moreaccurate, less laborious, having better performance fordetectionof such blood borne viral infectious diseases. This assay has also been shown to have better linear range and requires lesser sample volume than ELISAfor testing[14,15]. Therefore, hospitals and other diagnostics laboratories / centres have already opted and are still in the process of shifting more and more towards CLIAfor continuous loading of the sample(s), accurate and better results.

The findings of this study show that during the year 2012 to 2014, a total number of 532 CLIA as well as ELISA based immunodiagnostic kits of HIV-Ab, HCV-Aband HBsAgwere received. Out of these kits 113 (21.24%) were CLIA based and the rest 419 (78.76%) were ELISA based. But in the year 2015 and 2016, a total number of 509 CLIA as well as ELISA based immunodiagnostic kits of HIV-Ab, HCV-Ab and HBsAgwere received. Out of these kits 297 (58.35%) were CLIA based and the rest 212 (41.65) were ELISA based. It clearly indicates that there is a substantial growth of the CLIA technology and more growth is expected in the forthcoming time.

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