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A Retrospective Study on Trends of Serological Reactivity of Transfusion Transmitted Co-Infections among Blood Donors

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Abstract: ***Background: Transfusion Transmitted Infections (TTIs) pose a significant threat to the safety of blood transfusions. While individual pathogens have been extensively studied, Transfusion Transmitted Co-infections (TTCI), involving multiple infectious agents, remain relatively unexplored. This retrospective study aims to bridge this gap by investigating the prevalence and trends of TTCI among blood donors, considering factors such as sensitivity and specificity of screening tests, window periods, emerging pathogens, asymptomatic carriers, impact of geographical variation, and progression of other morbidities in donors/patients. Objective: To provide comprehensive insights into the trending patterns of serological reactivity of TTCI among a specified population by estimating the proportions of TTCI among blood donors and identify any existing demographical associations. Methodology: The study, conducted at SMS Medical College, Jaipur, accounting from January 2018 to December 2022, involving 1,57,834 blood donors. Routine screening for TTIs, in accordance with regulatory criteria, utilized ELISA and CLIA techniques. Results were analysed for serological reactivity, with statistical associations explored. Results: Among 3,41,076 donors, 2.88% exhibited serological reactivity to one or more TTIs. Mono-infections accounted for 97.47%, while dual and trio-infections were observed in 2.55% and 0.05% of cases, respectively. The most prevalent dual-infection was HIV and HCV (41.35%), and trio-infections included specific combinations like HBsAg+HCV+HIV. Statistical analysis revealed significant associations between demographic factors (age, gender) and TTI reactivity ($p < 0.05$). Conclusion: This study highlights a high prevalence of HIV, HBsAg, and HCV in combination among donors. The findings emphasize the importance of accurate donor screening to minimize TTIs, contributing to improved quality of life for both donors and recipients. The study underscores the need for ongoing efforts to enhance blood transfusion safety.***

Keywords: Transfusion Transmitted Co-infections, serological reactivity, blood transfusion safety

1. Introduction

The screening of blood donations for Transfusion Transmitted Infections (TTIs) is a fundamental practice in ensuring the safety of blood transfusions. Traditionally, emphasis has been placed on individual pathogens such as Hepatitis B virus (HBV), Hepatitis C virus (HCV), Human Immunodeficiency Virus (HIV), Syphilis and Malaria. Transfusion Transmitted Co-infections (TTCI) can be defined as the concurrent presence of multiple infectious agents in a single donor, presenting unique challenges in detection and management. The prevalence of Transfusion Transmitted Co-infections (TTCI) among blood donors remains a critical area of concern, However, Transfusion Transmitted Co-infections (TTCI) involving multiple pathogens have increasing attention due to their potential for heightened morbidity and mortality rates in transfusion recipients.

Despite advances in screening technologies, studies addressing the prevalence of co-infections among blood donors have been relatively limited. Existing data primarily focus on mono-infections, leaving a critical gap in our understanding of the dynamics of co-infections within the population like Sensitivity and Specificity of Screening Tests, Window Period, Emerging Pathogens, Asymptomatic Carriers, Impact of Geographical Variation & Enhancement in progression of other morbidities present in donor/patient.
The objective of the study is to provide comprehensive insights about the trending patterns of serological reactivity of Transfusion Transmitted Co-infections (TTCI) within the specified population by determining the proportions of Transfusion Transmitted Co-infections (TTCI) among blood donors and co-relate with any existing demographical associations.

2. Methodology

Study Method

This retrospective study was accounted from January 2018 to December 2022, from a documented registry database of blood donor transfusion transmitted infections (TTIs) records at Blood centre, SMS Medical College, Jaipur.

During the study period, a total of 3,41,076 blood donors were included in the analysis. Each donor underwent routine screening for transfusion transmitted infections (TTIs) in accordance with criterias as per Drugs and Cosmetics Act (Second Amendment), 2020 by Department of Health and Family Welfare. Blood samples were collected using standard venipuncture technique in blood donation area and was

processed within TTI screening laboratory of the blood centre at SMS Medical College & Attached Hospitals.

Inclusion Criteria

We included the clinically healthy individuals between 18-65 years of age with a body weight of above 50 kg and haemoglobin ≥12.5gm/dl without any significant medical or surgical history & maximally fulfilling criterias as per Drugs and Cosmetics Act (Second Amendment), 2020 by Department of Health and Family Welfare, were qualified for the donation process.

Exclusion Criteria

Donors as high risk patients with chronic diseases, intravenous drug users, dialysis patients, pregnant women, patients treated in thalassemia clinics, sexually transmitted disease clinics, sex workers and those not fulfilling criterias as per Drugs and Cosmetics Act (Second Amendment), 2020 by Department of Health and Family Welfare, were deferred from the donation process.

Enzyme-Linked Immunosorbent Assay (ELISA)

ELISA, a widely recognized serological assay, was employed for the invitro detection of specific serological screening markers against infectious agents present in human serum & plasma. Certified commercial specific ELISA kits were utilized to screen for the presence of antigens associated with each of transfusion transmitted infections (TTIs). The whole system had specific reagents, inventory & levels and their expiration dates which were monitored regularly.

Table 1: Screening Technique Parameters

Infective Agent	Technical Kit Specifications	Screening Serological Markers
Human Immunodeficiency Virus (HIV) – Type 1 & 2	Erba Lisa® Gen 4	HIV p24 Antigen
Hepatitis B Virus (HBV)	Hepalisa Ultra Gen 4	Hepatitis B Surface Antigen (HBsAg)
Hepatitis C Virus (HCV)	Erba Lisa® HCV Gen 3 (v2)	Anti HCV IgG antibodies against recombinant proteins - Core, NS3, NS4 & NS5
Syphilis (Treponema pallidum)	Rapid Immunochromatographic Assay	IgM & IgG Antibodies against recombinant antigen of Treponema pallidum
Malaria (Plasmodium parasite)	Malaria Card Antigen Immunoassay (Pf/Pv)	Pf. HRP-2 & Pv-LDH

Chemiluminescent Immunoassay (CLIA)

Complementing the ELISA screening, a Chemiluminescent Immunoassay (CLIA) technique was employed to further enhance the sensitivity of TTI detection. Few donor's samples & grey zone samples were screened using CLIA for confirmation. It offers a highly sensitive and specific method for quantifying specific sero-markers associated with infectious agents. Since calibrations is an important aspect of its quality control, for each new reagent lot, a master calibration with few multiple assays was regularly done.

Data Collection and Analysis

All data, including donor demographics, screening results and co-infection patterns were recorded in a secured electronic database. Data were compiled and analyzed with the help of MS-xl.

Statistical Methods

To assess the association between age and sex with TTI co-infection reactivity, chi-squared test and logistic regression analysis was conducted. Statistical analyses were performed using SPSS ver. 25 and descriptive statistics were calculated to elucidate the prevalence and distribution of TTCIs among blood donors. The significance level was set at $p < 0.05$. Odds ratios (OR) with 95% confidence intervals (CI) were computed to quantify the strength of associations.

Ethical Consideration: Ethical permission was taken from Ethics Committee of SMS Medical College.

Table 2: Association of Age and Gender with Proportions of Co-Infection TTIs (P<0.05 is considered significant) by Chi Square test

Age Group	Co-infection TTIs (Male)	Co- Infection TTIs (Female)	Total Co-infection TTIs	P-Value
<30	98	14	112	0.199
30- 50	82	08	90	0.159
>50	33	02	35	0.826
Total	213	24	237	

3. Results

A total of 3,41,076 blood donors were screened during the study period, out of which 9283 donors (2.88%) exhibited serological reactivity to one or more TTIs. The breakdown of infections is as follows: Mono-infections: 9041 cases (97.47%), Dual-infections: 237 cases (2.55%), Trio-infections: 5 cases (0.05%).

Among the dual-infections, the combination of HIV and HCV was the most prevalent, accounting for 41.35% of cases. Trio-infections were observed in 5 cases, with specific combinations as follows: HBsAg + HCV + HIV (n=3), HBsAg + HCV + syphilis (n=2). Statistical analysis revealed a statistically significant association between certain demographic factors like age & gender with TTI reactivity ($p < 0.05$).

Table 3: Proportions of Co-infections TTIs among blood donors

Dual/trio Infection TTIs	2018	2019	2020	2021	2022	Total No. of Cases
HIV + HCV	25	17	21	16	19	98 (40.50%)
HBsAg + HCV	12	13	14	16	17	72 (29.75%)
HBsAg + HIV	11	09	11	10	12	53 (21.90%)
HBsAg + Syphilis	02	01	01	-	02	6 (2.48%)
HCV + Syphilis	01	-	01	02	01	5 (2.07%)
HIV + Syphilis	-	01	-	01	01	3 (1.24%)
HBsAg + HCV + HIV	-	-	01	01	01	3 (1.24%)
HBsAg + HCV + Syphilis	01	-	-	-	01	2 (0.83%)

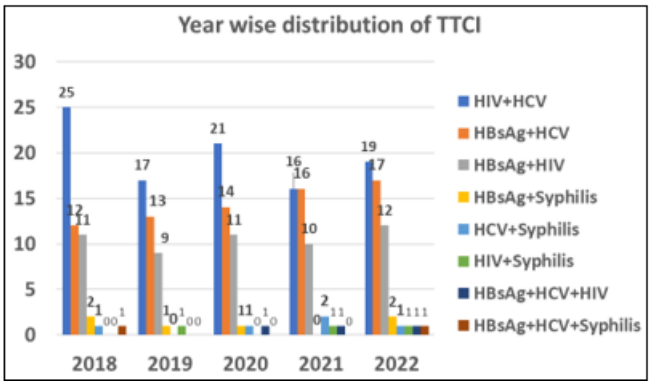

Figure 1: Year wise prevalence of TTCI

4. Discussion

Transfusion-transmitted co-infections have been an ongoing concern in blood safety measures. In the context of blood donation, this can involve the transmission of more than one infectious agent through a blood transfusion. Transfusion-transmitted co-infections (TTCI) in blood donors pose significant challenges in detection as well as in the management. The concerned critical gaps in dynamics of TTCIs are asymptomatic carriers of infectious agents, making it difficult to identify them during routine screening.

The window period, which is the time between infection and the ability of a screening test to detect the infection, is a critical aspect. We need to focus on narrowing this window period & are successful to some extent to reduce the risk of transfusion-transmitted infections during this phase. Attempts are in process to develop the more advanced screening technologies, such as nucleic acid testing (NAT) for a broader range of pathogens, to enhance sensitivity and reduce the window period. Nucleic acid testing (NAT) has been advocated in many countries to further minimize the risk of TTCIs, especially for viral infections like HIV and HCV, where early detection is critical. The implementation of NAT has proven effective in reducing the incidence of TTIs by detecting low viral loads that might escape conventional serological testing. The accuracy of screening tests is crucial, Understanding the sensitivity and specificity of these tests is critical to minimizing false negatives and false positives.

Holy Alomatu et al.[4] shows Coinfections found were HIV - HCV 0.4%, HIV - Syphilis 0.2%, HBV - Syphilis 1.2% and HCV - Syphilis 0.4% among 426 blood donors. Kaur H, Garg P, Kaur N et al.[2] estimates that out of 43037, 70 (4.04 %) had coinfections. HCV & HBV (28/70) was the most common combination, followed by HCV & HIV (20/70), HCV & syphilis (9/70), HIV & syphilis (5/70), HBV & syphilis (3/70) and HBV & HIV (1/70). Two donors had HIV, HCV & syphilis coinfections and two donors had HIV, HBV & HCV coinfections. Bhattar, Sonali et al.[5] showed among 220 sexually transmitted infections (STI) patients, Three were both HIV and syphilis positive and one was both HIV and HBV positive. Bhatti, Mahwish Majid et al.[9] states that, The frequency of co-infection of syphilis with HCV and HIV was 0.02% and 0.01%, respectively among 1,20,968 potential donors.

Co-infections of HIV and HCV significantly accelerates disease progression and complicate treatment as they are more likely to experience rapid progression of liver disease, even with antiretroviral therapy (ART). Similarly, co-infections of HBV and HCV can lead to worse clinical outcomes, increasing the risk of cirrhosis, hepatocellular carcinoma, and liver failure. Syphilis co-infection with HIV has been reported to increase both the severity and transmission rate of HIV. According to studies its associated with higher rates of neurological complications in HIV-positive patients. Further, the presence of malaria in blood transfusions, although less common in developed countries, can result in severe hemolytic anemia, particularly in immunocompromised recipients or neonates.

Continuous improvement in screening techniques and protocols is essential to minimize the risk of transfusion-transmitted co-infections (TTCIs) to ensure the safety of blood transfusions. The development of effective risk assessment tools is significant for identifying donors engaged in high-risk behaviours. Educating donors about the importance of disclosing relevant medical history and risk behaviours is equally important.

5. Conclusion

International guidelines recommend a strict and mandatory pre-donation questionnaire to exclude high-risk donors, particularly those with a history of high-risk sexual behaviour, intravenous drug use, or recent travel to malaria-endemic areas. Further, the introduction of pathogen reduction technologies (PRT) and the use of leukoreduction in blood components have been suggested as additional measures to reduce the burden of TTCIs.

By observing the results of this study having high prevalence in donors with HIV, HBsAg & HCV in combinations, must be strictly suspected clinically and screened technically. The ultimate focus of this study is to maximally reduce the transmission of TTIs via. accurate donor screening & provide risk free blood transfusion which directly or indirectly impacts on improving quality of life in donors as well as recipients.

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