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Evaluating the economic viability of hepatitis E virus serological screening among blood donors: A prospective study from India for advancing blood safety

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Abstract:

BACKGROUND: Hepatitis E virus (HEV) stands out as a significant transfusion-transmissible infection, yet it is not included in the screening protocols of many countries. The present study was conducted to assess the cost-benefit implications of incorporating HEV screening among blood donors which is one of the preventive strategies in reducing transfusion transmissible HEV.

METHODOLOGY: A decision tree model was prepared to assist the cost-benefit analysis. The serological screening cost of HEV was estimated based with fixed and variable cost. The cost of illness was estimated with direct and indirect cost. Net present value (NPV) and benefit-cost ratio (BCR) was used to measure the economic variability of screening HEV among the blood donors.

RESULTS: The unit cost of HEV IgM antibody screening is 1000 INR, and the unit cost of illness due to HEV infection is INR 80,122. The NPV and BCR is INR 6,73,001 and 1.7:1 for the probable transfusion-transmitted HEV infection that was averted by the screening of HEV among the blood donors.

CONCLUSION: Considering the risk of probable HEV transmission through blood transfusion, the study suggests that screening HEV among the blood donors is beneficial in averting transfusion-transmitted HEV infection.

Keywords:

Blood transfusion, cost-benefit analysis, hepatitis E virus

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Introduction

Globally, hepatitis E virus (HEV) is the main causative agent for most of the acute viral hepatitis infections. The typical mode of transmission involves the fecal-oral route, giving rise to outbreaks, epidemics, and sporadic cases in various regions globally.[1] To date, four primary genotypes of HEV have been identified as causing diseases in humans. Infections with HEV genotypes 1 (HEV1) and HEV2 are exclusive to humans and are transmitted through contaminated water and food. On the other hand, infections with genotypes 3 (HEV3) and 4 (HEV4) occur through the consumption of undercooked or raw pork and its derivatives.[2] Typically, the infection is self-limiting in the majority of immunocompetent individuals. However, instances of acute, fulminant, and liver cirrhosis have been documented. Notably, there is a substantial risk of chronic HEV infections among immunocompromised patients, especially with HEV3 and HEV4. These genotypes are naturally carried by swine and can be transmitted to humans

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through zoonotic means.[3] Besides being transmitted through the feco-oral route, this infectious disease has also been recognized as having the potential for transmission through blood transfusions, marking it as an emerging concern in the field of transfusion medicine.[4] Therefore, some of the developed countries were considering selective or universal screening of HEV among blood donors.[5]

To reduce and address the potential transmission of HEV through blood transfusion, it is crucial to implement specific precautions and measures. Currently, there is a scarcity of comprehensive studies and surveillance efforts aimed at identifying the cases of HEV transmission through blood transfusions. However, a limited number of reports from India have explored the prevalence and incidence of HEV ribonucleic acid (HEV RNA) among blood donors.[6-9] A study conducted at the Armed Forces Medical College investigated patients undergoing blood transfusions by monitoring the blood samples collected before and after the transfusion. Interestingly, no instances of Hepatitis E viremia were detected in either the pre- or post-transfusion samples.[10] Moreover, on follow-up, there was no seroconversion even after 3 months. This presents a challenge in determining the transfusion transmissibility of HEV1, a highly endemic virus. The potential risk lies in identifying viremia among blood donors, as this could contribute to the transmission risk through blood transfusions in the region.[6,8]

Screening for HEV among blood donors is not currently a policy, despite the high prevalence of HEV in India. It may be attributed to a deficiency in awareness, research, infrastructure, and budgetary constraints. Few of the European and some section of the Asian countries have a policy to universally screen HEV RNA among the blood donors.[11] In particular, the Netherlands has opinionated that an additional screening of HEV is not additionally expensive with respect to other transfusion-transmitted infections (TTIs) routinely tested in the country.[12] However, assessing the efficacy of HEV screening is essential to determine if the investment would yield the anticipated benefits in India.

Evaluating effectiveness can be approached in various ways, each with its own advantages and drawbacks. One such method is cost-benefit analysis, which assesses effectiveness in monetary terms. This approach is simpler and less complex compared to other economic evaluation techniques. When both the numerator and denominator of a cost-benefit analysis are quantified in monetary terms, evaluating whether the economic advantages of a program surpass its costs becomes crucial in determining its feasibility for implementation. However, there is a notable scarcity of information regarding the expenses associated with screening and diagnosis of HEV, especially in developing countries. Addressing this gap in knowledge is essential for informed policy-making before seriously considering the implementation of such programs.

Therefore, the study was carried out in estimating the cost-benefit of screening HEV among the blood donors to avoid transfusion-transmitted HEV infection to the transfusion recipients.

Methodology

The research took place within the transfusion medicine department affiliated with a medical college's tertiary care center, which annually collects approximately 15,000 blood donations. An approval from the institutional ethics committee was obtained before the initiation of the study (IEC no. 06/2020).

Method of screening

A total of 1939 blood donor participants were screened for anti-HEV IgM antibodies with DiaPro HEV IgM ELISA kit (Diagnostic Bioprobe SRL, Milano, Italy) as per the manufacturer protocol, which was mentioned in the previous finding by Sangthang *et al*.[13,14]

Cost of screening hepatitis E virus

The unit cost of screening encompasses both fixed and variable costs. Fixed costs include expenses related to instruments, facilities, information technology, salaries, electricity, and other permanent resources. On the other hand, variable costs encompass consumables, reagents, stationery, logistics, and other expenditures that vary based on the scale and frequency of screening activities. By analyzing both fixed and variable costs, a comprehensive financial outlay for the screening process was calculated. The parameters compiled from the hospital finance report and laboratory charge from the region.

Cost of Illness

The benefit of screening HEV was calculated as the averted medical cost due to HEV infection or illness, which is here termed as the cost of illness. The cost of morbidity and premature mortality can be broken down into medical, nonmedical expenditures, productivity losses, intangible expenses, and leisure losses, which is divided into:

1. Direct cost
    a. Direct medical cost – The expenses directly related to receiving medical care or expenses incurred by the health system are referred to as medical expenses. Such as expense on outpatient services, drugs, nursing care, and other cost related to diagnosis and treatment are included in the cost

   b. Direct nonmedical cost – Nonmedical costs are direct cost incurred in conjunction with the preventive activity of the health result of interest but for things and expenses not normally categorized as medical or health expenditure. Transportation, nutritional services, etc., were included in this cost.
2. Indirect cost: The cost of the time that HEV-infected inpatients and family careers miss at work represents the indirect economic burden. This study employed the human capital method, which first calculated the duration of lost work before translating it into a monetary value.[15] (The amount 1 $ is converted to its equivalent INR 82).

The cost of illness irrespective of the direct and indirect is however obtained from the previous report from the neighboring countries by Jiang *et al.*, (2017).[15]

Cost-benefit analysis

The financial strain or losses incurred due to HEV infections might be considered as a potential expense associated with treating individuals who have contracted HEV through blood transfusions, which is also considered as the benefit due to the averted HEV infection. A decision tree model was prepared to assist in the cost-benefit analysis [Figure 1]. In this model, a decision was made to serologically screen and not to screen HEV among the blood donors. Assuming the infectivity of contaminated blood component, an outcome of 100% infection through blood transfusion was proposed. Furthermore, there was a report of HEV-contaminated blood components with an infectivity rate of 50% among immunosuppressed-transfused patients as mentioned by Satake *et al.*,[16] the situation was otherwise taken into account for transmission outcome. The assessment of cost-benefit in screening HEV among blood donors is compared with a no-screening strategy.

The analysis involved assessing costs and benefits in monetary terms and consolidating them into summary metrics. Specifically, the cost-benefit analysis utilized the net present value (NPV) and benefit-cost ratio (BCR) as the key measures. A discount rate of 5% was applied, and the analysis considered an estimated 1-year value for the evaluation.[17] The NPV and BCR value of more than one could be considered as cost benefits.

Results

Out of 1939 donor screened for HEV, the prevalence of anti-HEV IgM antibody among the blood donors is 1.3% (n = 27), which shows that a significant number of blood donors were asymptomatically infected with HEV in the region. We assume that all the TTIs reactive sample has a potential risk of TTIs transmission through blood transfusion.

Cost analysis

The laboratory cost for one unit screening of anti-HEV IgM antibodies in our blood center was estimated as INR 1000/- only [Breakdown in Table 1] that may vary depending on the type of ELISA kit used, manufacturer, infrastructures, and the region. A total of 1939 blood donors were screened; it was estimated that INR 1,939,000/- was the cost for the technological intervention in this analysis. On the other hand, the unit cost of illness due to hepatitis E infection is INR 80,122/-

Table 1: Cost of serological screening of hepatitis E virus and cost of illness due to hepatitis E virus infection

Cost of parameters	Cost (INR)	Total cost (INR)
Cost of screening#		
Fixed cost	150	1000
Variable cost	850	
Cost of illness[15]*		
Direct economic burden		80,122
Direct medical	67,076	
Indirect medical	9020	
Indirect economic burden	4026	

*Cost of illness is extracted from the previous report by Jiang *et al.* (2017),[15]
#Hospital information system and different laboratories across the region

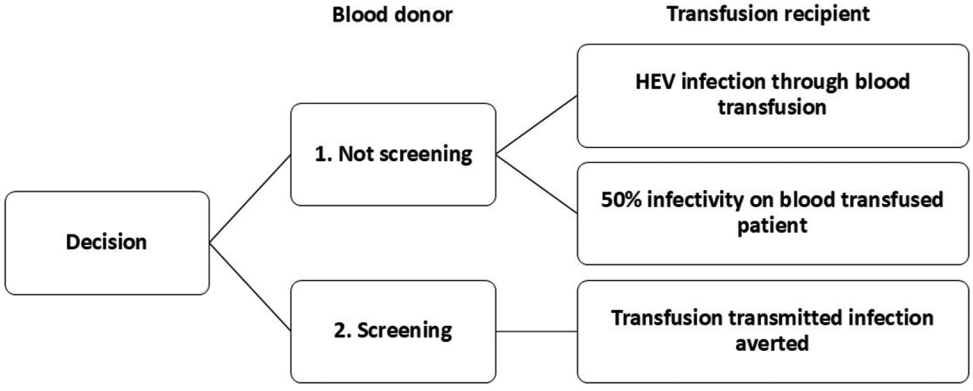

Figure 1: Decision tree model for serological screening of HEV among the blood donor

[Break down in Table 1] that the direct cost of illness is significantly higher than indirect cost of illness.

Cost-benefit analysis

The 27 HEV seropositive blood donor units would undergo a process of component separation, dividing them into three distinct units namely, packed red blood cells, plasma, and platelets. This separation increases the potential risk of transmission through different blood components. Therefore, if 27 blood units are infected, there is a potential risk that these units could transmit the infection to as many as 81 patients. The overall estimated cost of illness due to HEV infection would be up to INR 6,489,882, as shown in scenario one of Table 2. Assuming the infectivity of 50% among the immunocompromised patient as mentioned by Satake *et al*.,[16] 41 HEV-infected individuals cost of illness would be INR 3,285,002. The averted cost of illness due to HEV infection is regarded as the benefit though the screening of HEV among the blood donors.

The cost-benefit analysis for scenario one indicates an NPV of INR 758,480 at a discount rate of 5% for a 1-year follow-up. In addition, it demonstrates that the BCR in this regard is 3.34:1, demonstrating the value of funding HEV screening among blood donors. In contrast, the cost-benefit analysis for scenario two indicates an NPV of INR 673,001 at a discount rate of 5% for a 1-year follow-up. The BCR in this case is 1.7:1. In both cases, the investment serves to reduce the risk of HEV infection and transmission through blood transfusions.

Discussion

HEV is highly endemic in India causing outbreak and epidemics frequently that is commonly associated with HEV1. They were connected to flood during the monsoon season where sewage contamination to water source and due to the scarcity of water which led to consumption of unsafe water, especially in rural and urban slum areas.[18] With the detection of HEV RNA in water sample from different sources, the exposure to HEV among the population becomes high.[19,20] On the other hand, HEV4 has also been identified among the swine population in India which is known to cause severe and complicated diseases in other Asian countries.[21]

Table 2: Scenario of possible transfusion-transmitted hepatitis E virus infections

Scenario of HEV reactive blood unit	Unit possible of transmitting HEV infections (units)	Cost of illness due to TTIs (INR)
Three blood components with 100% infectivity	81	6,489,882
50% infectivity of blood transfused patients	41	3,285,001
Averted HEV blood component unit by screening	0	0

HEV=Hepatitis E virus, TTIs=Transfusion-transmitted infections

Given the varied sources of infection risk and the potential for disease spread, an individual in good health who regularly donates blood may not exhibit any detectable signs during the initial medical examination. This is based on the fact that the incubation period for HEV infection ranges from 2 to 8 weeks, and the infection itself is typically self-limiting in nature.[1]

The studies on the prevalence and the incidence of HEV infection among blood donors in India have documented varying findings across different regions of the country.[7,9,22] A report from Puducherry also suggests an economic evaluation for implementing the screening for HEV among the blood donors and that it could be expensive for mandatory screening.[23] Therefore, it is necessary to enhance hemovigilance efforts to promptly identify suspected cases of transfusion-transmitted HEV infections. In addition, it is crucial to develop effective protocols for managing blood donors found to be infected with HEV. Although the National Blood transfusion council dictates the deferral period of 12 months for HEV-infected blood donors, there could be more to cover the dynamics of HEV infection in both the donor and recipients.[24]

The screening for TTIs incurs costs and the inclusion of serological HEV screening will add on to the existing cost. Our finding indicates that a sum of rupees 1000 per unit will be needed for testing HEV, which closely matches with the report published from China.[25] In addition to that, an economic evaluation from the Netherlands suggests that an addition of nucleic acid amplification test for HEV screening among the blood donors is not expensive compared to other screening measures.[12] In contrast to that the use of serological screening may be more appropriate in rural and semi-urban areas. Our findings suggest that serological screening of HEV is beneficial at the cost of INR 80,122 for every averted case, which is equivalent to 44.3% of the national per capita income (as of 2021).[26]

In addition to that in scenario, one and two the net cost benefit is INR 4,550,882 and INR 1,346,001 respectively. Overall, serological screening of HEV among the blood donors appears to be beneficial from the extracted data and analysis.

The cost of illness may vary from region to region, which will also be affected by the severity of the infection and the co-morbidities in the patient. The cost of treatment is not uniform, and hence, there can be variation in the estimation, which is one of the limitations of the study.

Therefore, it is essential to study the disease dynamics among HEV-infected individuals and the economic burden among them to estimate the actual burden of the diseases across the globe. This will influence the other economic evaluation for suggesting an effective policy of screening HEV among the blood donors.

In addition, there is a need to explore and evaluate the molecular screening of HEV as a potential alternative or complementary method to serological screening. This approach is deemed highly effective for detecting active HEV infection, prompting a consideration for its comparative or substitutionary role in screening procedures. Furthermore, HEV is a vaccine preventable disease, it may be useful to further assess the vaccine requirement which could be effective in preventing HEV infection among the regular or repeated healthy voluntary blood donors.

Limitation

The assumption with respect to 50% infectivity among immunocompromised patient was reported by Satake *et al*.,[16] and it was based on the existing literature. The real-time scenario of the existing patient population in our center may be alike or different, which is the limitation and challenges for the study.

Conclusion

The study is the first economic evaluation of serological HEV screening among the blood donors, particularly in a highly endemic developing country. Considering the risk of probable HEV transmission through blood transfusion, our study suggests that screening HEV among the blood donors is beneficial in averting TTI. A collective observation and evaluation of the disease burden due to HEV infection across the globe would assist the policy-maker for better planning in preventing transfusion-transmitted infectious diseases.

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Conflicts of interest

There are no conflicts of interest.

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