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CHANGING CLINICAL LANDSCAPE OF HEPATITIS A IN CHILDREN: A COMPREHENSIVE SYSTEMATIC REVIEW AND CALL FOR UNIVERSAL VACCINATION IN INDIA

Paediatric Medicine

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ABSTRACT

Hepatitis A virus (HAV) infection, once considered a benign and self-limiting illness in children, is witnessing a paradigm shift in its clinical presentation and epidemiology in India. Improvements in sanitation, urbanization, and socio-economic conditions have led to a transition in the age of primary infection, making older children and adolescents more susceptible to symptomatic and occasionally severe forms of the disease, including acute liver failure (ALF). Despite the availability of safe and effective vaccines, hepatitis A is not included in India's Universal Immunization Program (UIP). This review explores the changing clinical spectrum of paediatric hepatitis A in India, the rising incidence of severe complications, and the compelling case for its inclusion in the national immunization strategy.

KEYWORDS

Hepatitis A virus, Acute Liver Failure, Universal Immunization Program

INTRODUCTION

Hepatitis A virus (HAV), an RNA virus of the Picornaviridae family, is a major cause of acute viral hepatitis globally. Hepatitis A, a highly contagious liver infection caused by the hepatitis A virus, remains a significant global health concern, particularly in regions with inadequate sanitation and hygiene practices (1,2). In India, a country marked by diverse socioeconomic strata and varying levels of access to clean water and sanitation, hepatitis A continues to pose a substantial burden on public health, especially among children (3). Traditionally considered a disease of developing countries, hepatitis A has long been perceived as a self-limiting illness with mild symptoms in children; however, recent epidemiological shifts indicate a changing clinical landscape, with an increased incidence of symptomatic cases and potential for severe complications in particularly in paediatric populations (4).

India, traditionally considered a high-endemicity region, has seen a changing pattern in hepatitis A epidemiology over recent decades. Previously, nearly all children acquired asymptomatic infection by age of 5years, resulting in lifelong immunity. However, with improved hygiene, sanitation, and living conditions, a growing number of children now escape early infection, becoming susceptible later in life when the disease is more likely to be symptomatic and severe. (5)

This epidemiological shift has important public health implications, especially considering the increasing number of reports documenting HAV-related acute liver failure (ALF) in Indian children. Despite these changes, the HAV vaccine remains absent from India's Universal Immunization Programme (UIP), even though it is recommended by the Indian Academy of Pediatrics (IAP). This review aims to examine the changing clinical landscape of hepatitis A in Indian children, highlighting the factors contributing to its persistence and exploring the rationale for universal vaccination as a proactive approach to disease prevention and control, considering the unique challenges and opportunities within the Indian context (6).

Changing Epidemiology Of Hepatitis A In India

1. Historical Perspective

Historically, hepatitis A was a ubiquitous childhood infection in India. High seroprevalence studies from the 1980s and 1990s revealed that over 90% of children had developed antibodies by the age of 10. (7) The infection was mostly asymptomatic, with only rare complications.

2. Emerging Trends

Recent studies indicate a significant decline in seroprevalence among young children, particularly in urban and semi-urban settings. Improvements in sanitation and hygiene practices, particularly in urban areas, have led to a decline in natural exposure to the virus, resulting in a growing pool of susceptible individuals, including older children and adolescents (8). This shift in susceptibility patterns has resulted in an increased incidence of symptomatic hepatitis A cases in older age groups, with a higher likelihood of severe complications, such as fulminant hepatic failure (9). (fig. no. 1) Moreover, the changing socioeconomic landscape of India has contributed to disparities in hepatitis A prevalence, with marginalized communities and those lacking access to clean water and sanitation bearing a disproportionate burden of the disease (10). Furthermore, the emergence of diverse hepatitis A virus genotypes and subtypes adds complexity to the epidemiological picture, potentially influencing disease severity and transmission dynamics. (11)

The intricate interplay of these factors necessitates a continuous monitoring of hepatitis A epidemiology in India to guide targeted interventions and optimize prevention strategies. Limited data may be available, as information is often collected during outbreak investigations (12). International travel, trade, and migration patterns can also impact the risk of outbreaks, particularly in regions with low or intermediate endemicity (13).

According to ICMR data, seroprevalence among children under 10 years in urban areas has dropped to nearly 50-60%. This shift has created a larger cohort of susceptible older children and adolescents who are more likely to experience symptomatic hepatitis, including complications. (12)

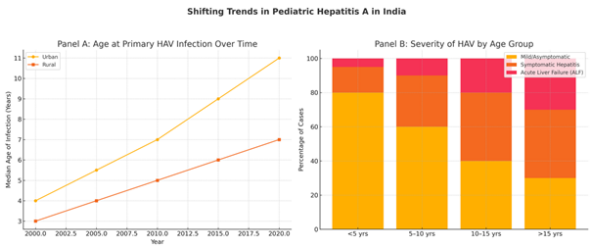

Fig. no. 1.: - Shifting Trends in Paediatric Hepatitis A in India: **Panel A**: Shows the increasing age of primary HAV infection over time, especially in urban areas. **Panel B**: Depicts the severity of disease increasing with age, including rising ALF in adolescents.

3. Regional Variation

Seroprevalence remains high in rural and underserved areas, but states like Kerala, Maharashtra, Delhi, and Tamil Nadu reports significant declines. (14) This heterogeneity poses challenges in crafting uniform public health policies but also highlights the need for preventive strategies that adapt to evolving trends.

Clinical Spectrum: From Asymptomatic To Acute Liver Failure

Hepatitis A virus infections manifest a wide spectrum of clinical presentations, ranging from asymptomatic or mild infections to severe, debilitating illnesses (15).

Typical Presentation

In children, hepatitis A traditionally presents with mild symptoms including fever, malaise, anorexia, nausea, abdominal discomfort, and jaundice. (15) Most cases resolve spontaneously within 1-2 weeks. These subclinical infections can contribute to the silent spread of the virus within communities, perpetuating the cycle of transmission. (15)

Severe And Atypical Manifestations

Emerging evidence from tertiary care centres in India shows an increasing number of HAV-related complications in children: (15)

1. Cholestatic Hepatitis

- Prolonged jaundice (>3 months) with pruritus, elevated ALP, and direct hyperbilirubinemia.
- Self-limiting; resolves without chronic liver damage but may require symptomatic treatment.

2. Relapsing Hepatitis

- Recurrence of symptoms (jaundice, elevated ALT) weeks/months after initial infection.
- Typically milder; resolves completely without long-term complications.

3. Autoimmune Hepatitis Triggered By HAV

- Rare, but HAV infection may induce autoimmune hepatitis in genetically predisposed individuals.
- Diagnosed by autoantibodies (ANA, ASMA, anti-LKM) and requires immunosuppressive therapy, if persistent.

4. Acute Liver Failure (ALF)

1. Rare (<1%), but risk increases with age or pre-existing liver disease.
2. Presents with encephalopathy, coagulopathy (INR >1.5) & jaundice (Raised bilirubin).
3. ALF has high mortality and often necessitates liver transplantation. Studies from institutions like AIIMS and PGIMER have reported HAV as a leading viral aetiology in paediatric ALF cases.
4. Mortality rates can be as high as 30-40% in such cases.

5. Extrahepatic Manifestations

- Extrahepatic manifestations, such as cutaneous vasculitis and cryoglobulinemia, can sometimes occur, with atypical manifestations occurring in 6-10% of cases (16).

Ascites, pleural effusion, and cholecystitis are extremely rare manifestations of hepatitis A virus infection (17)

Risk Factors For Severe Disease

- Older age at infection
- Underlying malnutrition
- Co-infections (e.g., hepatitis E)
- Genetic predisposition
- Delayed diagnosis and supportive care

The Case for Universal Vaccination

1. Global Guidelines and Practices

The WHO recommends HAV vaccination in regions with intermediate endemicity, where shifting age of infection increases morbidity. Several countries, including the USA, Argentina, China, and Israel, have incorporated HAV vaccination into their national schedules, resulting in a significant drop in incidence and complications.(11)

2. Indian Scenario

The Indian Academy of Pediatrics (IAP) recommends two doses of inactivated HAV vaccine at 12-15 months and 6 months later. However, the vaccine remains outside the UIP, making it accessible only to those who can afford it.(14)

3. Economic Considerations

While cost is a frequently cited barrier, economic analyses reveal that universal vaccination is cost-effective when factoring in hospitalization costs, parental work loss, and long-term health outcomes. The price of HAV vaccines has also declined significantly, making national procurement viable.

4. Vaccine Safety And Efficacy

HAV vaccines are highly immunogenic, with seroconversion rates exceeding 95% after the second dose. They have excellent safety profiles and provide long-lasting protection. (4)

Current Vaccination Strategies And Their Limitations

Current hepatitis A vaccination strategies vary across countries, with some recommending universal vaccination for all children, while others focus on vaccinating high-risk groups.

High-risk groups often include travelers to endemic areas, individuals with chronic liver disease, men who have sex with men, and people who use illicit drugs. The hepatitis A vaccine is highly effective in preventing infection, with studies demonstrating seroprotection rates of over 95% after two doses. [4] However, challenges remain in achieving high vaccination coverage, particularly in resource-limited settings where access to vaccines may be limited. Factors such as vaccine cost, logistical constraints, and lack of awareness can hinder vaccination efforts. Furthermore, some individuals may not respond to the vaccine, particularly those who are immunocompromised or have underlying medical conditions.

The Rationale For Universal Vaccination

The implementation of universal hepatitis A vaccination programs in India holds significant promise for reducing the disease burden, preventing outbreaks, and improving overall public health outcomes. Vaccination offers a safe and effective means of achieving herd immunity, protecting not only vaccinated individuals but also those who are unable to receive the vaccine due to medical contraindications. (5) Evidence from countries that have implemented universal hepatitis A vaccination programs demonstrates a substantial decline in disease incidence, hospitalizations, and associated healthcare costs. In the Indian context, where sanitation and hygiene practices vary widely, and the risk of exposure to hepatitis A virus remains high, universal vaccination can provide a critical layer of protection, particularly for vulnerable populations.

Table 1. Systematic Review Table: Hepatitis A in Children – Recent Evidence from India (1,3,14)

Study	Year	Region	Population	Findings
Bansal et al.	2020	North India	1,000 children	Rising incidence in adolescents; shift in age of infection
Sharma et al.	2021	West India	450 hospitalized cases	Hepatitis A common cause of acute hepatitis; 80% unvaccinated
ICMR Survey	2022	Pan-India	20,000 serum samples	Declining seroprevalence in <10 years; supports vaccination
Kumar et al.	2023	South India	600 school-aged children	35% susceptibility to HAV; outbreak linked to low hygiene

Patel et al.	2024	East India	300 pediatric inpatients	Moderate to severe hepatitis in unvaccinated children

Recent Indian studies (table 1) indicate a marked epidemiological shift in hepatitis A infection from early childhood to adolescence, with an increasing number of symptomatic and hospitalized cases in older children. (1,3,14) The majority of these patients are unvaccinated, emphasizing the gap in preventive strategies.

The ICMR serosurvey further highlights declining natural immunity due to improved sanitation—ironically increasing vulnerability in early life. This shift makes a strong case for integrating HAV vaccination into the Universal Immunization Program (UIP).

Outbreaks in school settings and urban slums reflect poor awareness and inadequate preventive infrastructure. The burden of hospitalization and economic impact on families further underscores the need for a universal vaccination approach. These findings collectively support the urgent need to revisit current vaccination guidelines and advocate for the inclusion of hepatitis A in India's national immunization policy.

India, with its high population density and suboptimal sanitation infrastructure, faces a significant burden of hepatitis A. While the exact seroprevalence rates vary across regions, studies have shown that a large proportion of children in India are infected with hepatitis A before adulthood (18). Furthermore, frequent outbreaks of hepatitis A have been reported in India, particularly in urban slums and areas with poor sanitation (19). These outbreaks not only cause significant morbidity and mortality but also disrupt economic productivity and strain healthcare resources. Given the high burden of hepatitis A in India and the limitations of targeted vaccination strategies, universal vaccination of children against hepatitis A is a compelling public health intervention. Low HAV vaccination coverage in India leaves a significant proportion of children unprotected. This contributes to a high burden of hospitalizations, especially among unvaccinated individuals. (fig. no. 2)

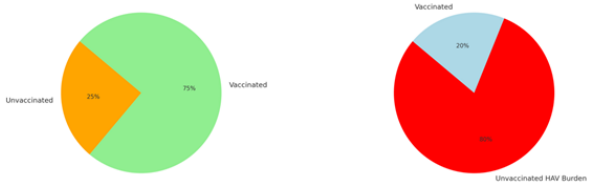

Fig. No. 2.: Highlights low HAV vaccination coverage and a high burden of hospitalization among unvaccinated children.

Universal vaccination can provide direct protection to vaccinated individuals, as well as indirect protection to unvaccinated individuals through herd immunity. Moreover, universal vaccination can prevent outbreaks, reduce the overall disease burden, and improve the health and well-being of children in India. Economic analyses have suggested that universal hepatitis A vaccination is cost-effective in India. Therefore, implementing universal hepatitis A vaccination in India is not only ethically justifiable but also economically sound (20).

Universal vaccination strategies are essential in areas where sanitation challenges increase the risk of exposure. Sustained commitment from public health authorities is needed to address these issues (21). India struggles to increase coverage of routine vaccination (22). Therefore, integrating the hepatitis A vaccine into the national immunization program would be crucial for success.

Efficacy Of Hepatitis A Vaccines

Hepatitis A vaccines have been proven to be safe and effective in preventing hepatitis A infection. Both inactivated and live-attenuated hepatitis A vaccines are available, and both types have demonstrated high levels of immunogenicity and protection (23).

Inactivated hepatitis A vaccines typically require two doses, administered six to twelve months apart, to induce long-term immunity. Live-attenuated hepatitis A vaccines, which are primarily used in some countries, offer the advantage of a single-dose schedule. Clinical trials have shown that hepatitis A vaccines can induce protective antibody responses in over 95% of recipients, providing long-lasting immunity against hepatitis A infection.

Real-world studies have also demonstrated the effectiveness of hepatitis A vaccines in reducing the incidence of hepatitis A and preventing outbreaks. The duration of protection conferred by hepatitis A vaccines is estimated to be at least 20 years, and possibly lifelong. The efficacy of hepatitis A vaccines has been further demonstrated in various populations, including children, adolescents, and adults.

Cost-Effectiveness Analysis Of Vaccination

Economic evaluations of hepatitis A vaccination programs have consistently demonstrated their cost-effectiveness, particularly in countries with intermediate or high endemicity. (24) (table no.2) Cost-effectiveness analyses typically compare the costs of vaccination programs with the costs associated with managing hepatitis A cases and outbreaks, including medical care, hospitalization, and lost productivity.

Several studies have shown that universal hepatitis A vaccination is a cost-effective strategy for preventing hepatitis A and reducing its associated morbidity and mortality. (11) In countries with high endemicity, universal hepatitis A vaccination can lead to substantial cost savings by preventing a large number of hepatitis A cases and outbreaks. Even in countries with intermediate endemicity, universal hepatitis A vaccination can be cost-effective. (12)

Table 2. WHO Recommendations On Hepatitis A Vaccination (24)

HAV Endemicity	WHO Recommendation	Target Groups (if applicable)
High	Defer large-scale vaccination	Not required – most infected asymptomatically in childhood
Intermediate	Recommend large-scale vaccination (cost-effective)	General population
High (with improving SES)	Recommend large-scale vaccination due to increased susceptibility in adults	General population
Low / Very Low	Targeted vaccination for individual health benefit	- Travelers to endemic areas - Lifelong transfusion recipients - Men who have sex with men - Chronic liver disease patients - Workers in contact with non-human primates - People who inject drugs

The cost-effectiveness of hepatitis A vaccination programs can be further enhanced by integrating them with other routine childhood immunization programs. The substantial economic burden associated with managing outbreaks underscores the economic rationale for investing in preventative measures like universal vaccination. By preventing hepatitis A infections and outbreaks, vaccination programs can reduce healthcare costs, improve productivity, and promote economic development.

Barriers To Implementation

1. Policy Gaps

India's UIP prioritizes diseases with high mortality and outbreak potential. Although HAV has a lower overall fatality rate, its increasing burden and preventability through vaccination warrant reconsideration.

2. Surveillance Limitations:

Lack of robust HAV surveillance data, especially in rural areas, limits policy makers' ability to assess the true burden. There is a need for enhanced data collection and integration into national disease monitoring systems.

3. Public Awareness

Limited awareness among caregivers and some healthcare providers about the changing risk profile of hepatitis A contributes to low vaccine uptake in private practice settings.

Recommendations

1. **Inclusion In UIP:** Consider pilot introduction of HAV vaccine in urban districts with low seroprevalence and high case burden.
2. **Enhanced Surveillance:** Establish a national hepatitis A registry

to collect data on incidence, complications, and outcomes.

3. **Cost Subsidization:** Negotiate bulk pricing and government subsidies to reduce vaccine costs.
4. **Public Education:** Launch awareness campaigns emphasizing the changing nature of hepatitis A and the need for vaccination.
5. **Targeted Catch-up Programs:** Immunize school-aged children who missed early vaccination opportunities.

CONCLUSION

Hepatitis A is no longer an innocuous childhood illness in India. With changing socio-economic dynamics, a larger proportion of children are acquiring the infection at an older age, resulting in more severe disease and increased risk of acute liver failure. This evolving clinical landscape necessitates a re-evaluation of India's immunization policy. Including hepatitis A vaccine in the Universal Immunization Programme would be a timely, evidence-based intervention that could prevent unnecessary morbidity and mortality in the pediatric population.

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