Hepatitis E Virus Outbreak among Tigray War Refugees from Ethopia, Sudan

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DOI: https://doi.org/10.3201/eid2901.221495

To the Editor: We read with interest the article by Ahmed et al. on a large hepatitis E virus (HEV) outbreak among refugees from Ethiopia in Sudan, underscoring the challenges in controlling HEV outbreaks (*1*). As part of the rationale for not using HEV vaccine, the authors state that no data on virus genotype were available from cases and "the success of vaccination is dependent on the HEV genotype." We believe that current evidence contradicts this assertion.

Evidence to date suggests that all major HEV genotypes that infect humans (genotypes 1–4) show cross-protection with a single serotype. Several pieces of data indicate that the only available and licensed vaccine (Hecolin; Wantai BioPharm, https://www.ystwt.cn), which contains recombinant partial capsid protein of HEV genotype 1, offers protection against infection with other genotypes. Studies in rhesus macaques have demonstrated protection by this vaccine against infection with genotypes 1 and 4 (*2*). In a large phase 3 trial of Hecolin, of the 23 persons who had HEV infection (1 in vaccine group and 22 in placebo group), viral genotype was identified in 13 placebo group patients. Of those, 12 were genotype 4 and 1 was genotype 1, providing evidence of protection against genotype 4 infection, a heterologous strain to that in the vaccine (*3*). Furthermore, in vitro data also support cross-protection across HEV genotypes (*4*).

A safe and efficacious vaccine is available and has been recommended for use as an outbreak control tool by the World Health Organization Strategic Advisory Group of Experts on Immunization (*5*), and this recommendation does not refer to virus genotype. Because empirical evidence from in vitro studies, nonhuman primate challenge studies, and a phase 3 clinical trial all point to cross-genotype protection, we believe that the lack of genotyping data during an outbreak should not prevent or delay the use of the HEV vaccine.

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In Response: We appreciate the insightful comments from Azman et al. on use of licensed hepatitis E virus (HEV) vaccine (Hecolin; Wantai BioPharm, https://www.ystwt.cn) for outbreak control regardless of virus genotype (*1*). We share their concern about the need for timely use of effective outbreak control measures, particularly among those at high risk for illness and death, such as forcibly displaced populations in humanitarian camps. We also agree that vaccines are an effective tool for prevention and control of outbreaks, including HEV (*2*).

When we confirmed an HEV outbreak among refugees from Ethiopia in east Sudan, according to the World Health Organization (WHO) recommendation, the National Immunization Technical Advisory Groups of Sudan convened an emergency meeting to discuss the feasibility of deploying HEV vaccine. After considering the WHO position paper about the use of HEV vaccine (*3*) and careful discussion, they raised several concerns about introducing the vaccine. These concerns included the limited evidence on efficacy and safety data in pregnant women, persons <16 years of age, the elderly (>65 years of age), and persons with underlying diseases (e.g., liver disease) or conditions such as immunosuppression (*3*). Of particular concern were children and pregnant women in humanitarian crisis, who are most at risk during HEV outbreaks (*4*). A major concern was that, according to

the WHO statement on the vaccine, "there are no data on specific protection afforded by the HEV 239 vaccine against genotype 1, 2, or 3 HEV infection." Therefore, the final recommendation was to invest more resources toward improving water, sanitation, and hygiene interventions until further evidence is available. In addition, several diseases prevalent among displaced populations in Sudan are preventable through water, sanitation, and hygiene interventions (*5*). These infections include waterborne diseases such as HEV and cholera (*2*,*6*); vectorborne diseases such as Chikungunya, dengue, and Rift Valley fever (*5*,*7*); and measles, meningitis, and poliomyelitis (*5*).

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DOI: https://doi.org/10.3201/eid2902.221796