Vaccine effectiveness against COVID-19 in-hospital mortality by HIV status across SARS-CoV-2 variants

Seth Inzaule
WHO
Geneva, Switzerland

Disclosure: None
Background

- COVID-19 vaccines have proven to be efficacious in attenuating severe and fatal disease
  - There is however limited data among immuno-compromised patients such as people living with HIV (PLHIV) as they are usually underrepresented or excluded in trials

- Due to immune dysfunction PLHIV have comparatively reduced immune responses to vaccines including Hepatitis B and influenza vaccines
  1. Remschmidt C et al Influenza vaccination in HIV-infected individuals: systematic review and assessment of quality of evidence related to vaccine efficacy, effectiveness and safety, 2014
  2. Tian Y et al Immune Response to Hepatitis B Virus Vaccine Among People Living With HIV: A Meta-Analysis Frontiers Immunology 2022

- Studies however conflict on the effectiveness of COVID-19 vaccines among PLHIV compared to HIV negative populations with some studies showing equivalent protectiveness while others showing a weakened and shorter vaccine response among PLHIV

- There is therefore a need for more studies to assess COVID-19 vaccine effectiveness among PLHIV
Objectives

• To determine the effectiveness of COVID-19 vaccine in reducing in-hospital mortality among PLHIV across the different SARS-CoV-2 variant waves

• To determine whether there is differential attenuation of in-hospital mortality by COVID-19 vaccines among PLHIV compared to HIV negative population across the different SARS-CoV-2 variant waves
Methods

• Anonymized individual-level clinical data from hospitalized patients from 41 countries, submitted to the WHO Global Clinical Platform during pre-Delta, Delta and Omicron predominant period
  • Predominant period was defined as when >90% of the cases were infected with the variant

• Inclusion Criteria: All patients, regardless of age, with known HIV status and admitted to a hospital or health facility with laboratory-confirmed or suspected COVID-19 were included in the analysis

• Reported variables included demographics, HIV status, comorbidities, disease severity, vaccination and outcomes. Vaccination was defined as having at least one dose of any SARS-CoV-2 vaccine.

• Data collection tools: clinical data were collected using the WHO Case Report Form (CRF) and entered directly into the WHO Clinical Platform hosted on OpenClinica or, for data already entered in a local system or database, these datasets were transferred and harmonized to the WHO CRF data dictionary. The CRF has been translated into 7 languages

• Statistical Analysis: Bivariate and regression analyses were conducted to determine the effect of vaccination in reducing in-hospital mortality (Proportional Hazard model) by HIV status. The models were adjusted for potential correlation for clustering at the country level. Covariates were considered for inclusion in the model when >80% reported data was not highly correlated with other variables using a correlation matrix threshold of >0.8
Main findings

• 159,082 patients hospitalized with COVID-19 during pre-delta, delta and omicron periods (up to Oct 2023) with information on HIV and COVID-19 vaccination were included in the analysis
  • 86,221 (54.2%) Pre-Delta
  • 34,968 (22.0%) Delta
  • 37,893 (23.8%) Omicron

• This included 10,147 (6.4%) data on PLHIV: 3875 (4.5%) during the pre-delta, 2531 (7.2%) during delta period and 3741 (9.8%) during the omicron period

• Overall, 24% of the patients had received at least one dose of vaccine
  • Pre-Delta (4.5%); 35.7% among those HIV negative vs 11.1% among PLHIV (p<0.001)
  • Delta (34%); 13.2% among those HIV negative vs 12.5% among PLHIV (p=0.2045)
  • Omicron (39%); 41.1% among those HIV negative and 28.6% among PLHIV (p<0.001)
Impact of vaccination on in-hospital mortality among PLHIV across pre-delta, delta and omicron variant periods

Vaccinated PLHIV had a 40-64% reduction in in-hospital deaths compared to the unvaccinated across the three variant waves.
Impact of vaccination on in-hospital mortality by HIV status across pre-delta, delta and omicron variant periods

Compared to the unvaccinated HIV negative group, vaccinated HIV negative persons had 38-41% reduction in in-hospital deaths across the variant waves but mortality risk remained higher among PLHIV especially in the unvaccinated.

Mortality rates during pre-delta, delta and omicron variants
Unvaccinated HIV neg: 20%, 19%, 8.4%
Vaccinated HIV neg: 16%, 15%, 8.2%
Unvaccinated PLHIV: 30%, 25%, 19%
Vaccinated PLHIV: 21%, 18%, 15%

Adjusted Odds Ratio (95% CI)

Pre-delta
- HIV negative unvaccinated: 1.0
- HIV negative vaccinated: 0.60 (0.56-0.63)
- PLHIV vaccinated: 1.76 (1.18-2.64)
- PLHIV unvaccinated: 1.97 (1.81-2.16)

Delta
- HIV negative unvaccinated: 1.0
- HIV negative vaccinated: 0.62 (0.57-0.68)
- PLHIV vaccinated: 0.69 (0.47-1.03)
- PLHIV unvaccinated: 1.75 (1.56-1.95)

Omicron
- HIV negative unvaccinated: 1.0
- HIV negative vaccinated: 0.59 (0.53-0.65)
- PLHIV vaccinated: 1.44 (1.08-1.93)
- PLHIV unvaccinated: 2.43 (2.10-2.81)
Limitations

- Study did not account for other factors known to impact COVID-19 vaccine induced immune response among PLHIV including, type of vaccine, frequency and number of vaccine doses and past SARS-CoV-2 infections as this data was either limited or unavailable.

- Our study only included hospitalized populations who are likely to have had severe cases of the disease and may not be a representative of all patients especially those with benign cases.
Conclusions

• Overall COVID-19 vaccination was associated with 40-64% reduction in risk of death among hospitalized PLHIV compared to the unvaccinated across the different SARS-CoV-2 variant waves.

• Compared with the unvaccinated HIV negative populations, HIV negative vaccinated patients had also ~40% reduction in risk of in-hospital deaths across the different variant waves but the risk was high among PLHIV especially among the unvaccinated cases.

• Overall findings continue to emphasize the need to implement WHO recommendations for giving booster vaccine doses for all PLHIV particularly those with low CD4 counts.

Acknowledgements

All patients, institutions and networks contributing data to the WHO Global Clinical Platform

WHO HQ team: Silvia Bertagnolio, Ronaldo Silva, Soe Soe Thwin, Nathan Ford, Marco Vitoria, Meg Doherty, Janet Diaz
NICD, South Africa: Waasila Jassat, Richard Welch

WHO Clinical Advisory Group

Chair: Rashan Haniffa, University College Hospital, United Kingdom; Chair: Robert Fowler, Sunnybrook Health Sciences Centre, Canada
Bin Cao, China-Japan Friendship Hospital, China
Gail Carson, United Kingdom
John Amuasi, Kwame Nkrumah University of Science and Technology, Ghana
Lee Wallis, University of Cape Town, South Africa
Linden Baden, Harvard Medical School, USA
Lucille Blumberg, NICD, South Africa
Margaret Herridge, Canada
Michael Hughes, Harvard TH Chan School of Public Health, United States of America
Michael Jacobs, Royal Free London NHS Foundation Trust, United Kingdom
Natalia Pshyenshya, Rostov State Medical University (RSMU), Russia
Paolo Bonfanti, Hospital San Gerardo, Monza
Pisake Lumbiganon, Khon Kaen University, Thailand
Richard Kojan, ALIMA & University of Kinshasa, Democratic Republic of Congo
Roger Paredes, Departament de Salut, Generalitat de Catalunya, Spain
Sabue Mulangu, Institut National de Recherche Biomedical, Democratic Republic of Congo
Shabina Ariff, Department of Pediatrics & Child Health, Ministry of Health, Pakistan
Tim Uyeki, Centres for Disease Control and Prevention, United States of America
Yaseen Arabi, King Saud University, Saudi Arabia
Yee Sin Leo, National Centres of Infectious Diseases, Ministry of Health, Singapore
Yinzhong Shen, Fudan University, China