

# WORLD CONGRESS ON RHEUMATIC HEART DISEASE

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**Title:** INVESTIGATING BENZATHINE PENICILLIN PROPHYLAXIS IN RHEUMATIC HEART DISEASE MORTALITY: A VERBAL AUTOPSY STUDY

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**Background & Aims:** Rheumatic Heart Disease (RHD) continues to be a major contributor to illness and death among children in low-income countries, such as Malawi. The administration of Benzathine Penicillin G (BPG) has been proven effective in enhancing the survival rates of RHD patients and preventing recurrent Rheumatic Fever. However, there is a concerning rise in reports of cardiovascular collapse following these injections. The study aimed to use verbal autopsy to gain insights into the relationship between injectable Benzathine Penicillin prophylaxis and RHD fatalities, contributing to improved management of patients and possible prevention fatalities.

**Methods:** We conducted interviews at Kamuzu Central Hospital (KCH) and Queen Elizabeth Central Hospital (QECH) in Malawi to investigate common trends in mortality related to RHD and the administration of BPG. Between February 2019 and February 2022, we prospectively enrolled 200 RHD patients, aged 4 to 18 years, receiving care at KCH and QECH. We identified 30 deaths by following up on parental reports and contacting guardians of patients who missed appointments. The thirty guardians provided a written informed consent and participated in the interviews. The interviews utilized a verbal autopsy questionnaire adapted from the World Health Organization's International Standard Verbal Questionnaire and translated into the local language. An experienced clinician conducted the interviews, which were recorded, summarized, and translated into English. Two reviewers analyzed each interview, and the study database was reviewed for information on disease severity.

**Results:** Twenty (67%) out of 30 deaths were female, 10 (33%) were male, which is in line with the overall distribution of RHD in our clinic. Age at death was 7- 18 years, with an average of 11.8 years and a median age of 11.5 years. Seventeen (57%) patients died at a hospital facility while 13 (43%) died at home. Three patients died within 2 minutes of Benzathine Penicillin Injection, representing 10%. All patients who died had severe RHD. Guardians did not describe signs suggestive of anaphylaxis, but rather, described an episode of collapse. Two of these were strongly suspected to have had a vagal reaction to BPG in severe disease. The third patient was newly diagnosed in severe heart failure and had progressive respiratory symptoms. Three patients died within 48hrs of BPG Injection. While the guardians associated the deaths to the injection, they were likely unrelated. Of these, 2 died in the hospital as they were admitted in heart failure. The third patient died at home 48hrs after Benzathine Injection, thought to have possibly developed arrhythmias and possible electrolyte imbalance as she had developed diarrhea. Of the 80% that died after 48hrs, 11 were suspected to have had arrhythmias that contributed to their demise. One developed endocarditis. Four (13%) were likely having worsening heart failure, 1 had a stroke, and the rest had superimposed conditions including malaria (1), infection(4), pneumonia(1) and gastroenteritis(3) with possible electrolyte imbalance (3) and gastrointestinal bleeding (1).

**Conclusions:** Children with RHD in Malawi have a high mortality rate. BPG injections are linked to mortality in patients with severe RHD, likely due to a vasovagal compromise. In patients with severe RHD and increased risk of cardiovascular compromise (severe aortic insufficiency, mitral stenosis, aortic stenosis, EF <50% or severe symptoms), substituting oral for injectable Penicillin may prevent BPG-related mortalities.