Etiological Agents of Diarrheal Diseases Detected Among Under-5 Deaths in Manhiça and Quelimane Districts, Mozambique in the CHAMPS Network, 2017-2021

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INTRODUCTION
- Diarrhea is the 3rd leading cause of mortality in children under-5 globally, being responsible for 525,000 deaths worldwide each year [1,2];
- In Mozambique, The Global Enteric Multicenter Study-GEMS (2007-2012) showed that Rotavirus, Cryptosporidium, enterotoxigenic Escherichia coli, Shigella and Adenovirus 40/41 were associated with moderate-to-severe diarrhea in children <2 years of age in Manhiça district [3], however, there is a scarcity of studies assessing the specific role of etiologic agents of diarrhea in children under-5 mortality;
- The Child Health and Mortality Prevention Surveillance (CHAMPS) aims to investigate causes of death of children under-5, trough post-mortem Minimally Invasive Tissue Sampling (MITS);
- In this analysis, we aim to describe the etiologic agents causing diarrhea in deceased children in Manhiça and Quelimane districts, Mozambique in CHAMPS study from January 2017 - December 2021.

Keywords: Diarrhea, Etiology, Deceased children.

METHODOLOGY
- Stillbirths and children <5 years of age at the time of death were enrolled in CHAMPS study (www.champshealth.org) ongoing in Manhiça and Quelimane districts from January 2017-December 2021;
- After death notification, families of eligible stillbirths/deceased children were approached for consent and MITS was performed within 24 hours;
- Rectal swabs samples were collected and Real-time polymerase chain reaction for detection of over 40 enteric pathogens was performed using TaqMan Array Cards (TACs, Thermo Fisher Scientific);
- A panel of experts determined causes of deaths by reviewing all available data including parasitology, microbiology and pathological results, clinical information from medical records, and verbal autopsies (fig 1);
- Data regarding stillbirths was excluded from this analysis, since the causes of death typically reflect maternal conditions [4].

RESULTS

1. Participants enrollment
Overall, 467 MITS were performed, of which 335 were from <5 years old. Among these (n=335), 196 were neonates (from birth to <28 days), 56 infants (28 days to <12 months) and 32 were older children (12-59 months).

2. Enteric pathogens detection
- At least one enteric pathogen was detected in 92% (307/335) of all deaths;
- When compared with viruses and protozoa, the bacterial pathogen predominated (98%), with frequent detection of Enteraggregative E. coli (EAEC) (45%), Aeromonas spp. (37%) and Entovirus (14%) (Fig 2).

3. Cause of death attribution
- From the 335 deaths, 276 (82.4%) were attributed to a cause of death;
- Diarrhea was the third leading cause of death with 8.7% (24/276) after Severe birth asphyxia (9.8%, 27/276) and Respiratory distress syndrome of the newborn (9.4%, 26/276);
- From the 24 children with diarrhea as cause of death, 1 was a neonate, 11 were infants and 12 were older children (Table 1).

Table 1. Age distribution of Deaths with MITS procedure, causes with Descr; results, deaths with enteric pathogen detected and deaths with diarrhea as cause of death, in Manhiça and Quelimane districts from 2017-2021.

<table>
<thead>
<tr>
<th>Age at death (months)</th>
<th>All deaths</th>
<th>Deaths with diarrhea</th>
<th>Deaths with at least one enteric pathogen detected</th>
<th>Deaths with diarrhea in the causal chain of cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonate</td>
<td>196</td>
<td>159 (57.6)</td>
<td>139 (54.7)</td>
<td>14 (2)</td>
</tr>
<tr>
<td>Infant</td>
<td>56</td>
<td>46 (16.7)</td>
<td>44 (16.7)</td>
<td>11 (45.8)</td>
</tr>
<tr>
<td>Children (12-59)</td>
<td>83</td>
<td>71 (25.7)</td>
<td>71 (25.7)</td>
<td>12 (50)</td>
</tr>
<tr>
<td>Total</td>
<td>335</td>
<td>276 (254)</td>
<td>241 (72.2)</td>
<td>16 (16.5)</td>
</tr>
</tbody>
</table>

4. Enteric pathogens in the causal chain of deaths due to Diarrhea.
From the 24 deaths where diarrhea was the cause of death:
- 8.3% (2/24) were caused by Rotavirus A;
- 4% (1/24) were due to Vibrio cholera;
- 1 (4%) by Salmonella spp.;
- 1 (4%) by Enteropathogenic E. coli (EPEC);
- 79.2% (19/24) were due to unspecified pathogens.

CONCLUSIONS
- Diarrhea was an important cause of death being responsible for 8.7% of the deaths;
- Rotavirus A, Vibrio cholerae, Salmonella spp and EPEC were in the causal chain of deaths due to diarrhea;
- Although, EAEC and Aeromonas spp were detected in high rates, they had low impact in the causal chain of deaths due to diarrhea;
- A high proportion of the diarrhea was due to unspecified pathogens, therefore a continuous molecular based surveillance of enteric pathogens is required to address the specific role of these pathogens in children under-5 mortality.

REFERENCES


Fig 1. Flowchart of determination of Cause of Death process in CHAMPS network [2].

Fig 2. Frequency of diarrheal pathogens detected in deceased children in Manhiça and Quelimane districts from 2017-2021.