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Prevalence and fluid management of dehydration in children without diarrhoea admitted to Kenyan hospitals: A multi-site observational study.

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Prevalence and fluid management of dehydration in children without diarrhoea admitted to Kenyan hospitals: A multi-site observational study.

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ABSTRACT

Objectives: To examine the prevalence of dehydration without diarrhoea among admitted children aged 1-59 months and describe fluid management practices in such cases.

Design: A multi-site observational study that used routine in-patient data collected prospectively between October 2013 and December 2018.

Settings: Study conducted in 13 county referral hospitals in Kenya.

Participants: Children aged 1-59 months with admission or discharge diagnosis of dehydration but had no diarrhoea as a symptom or diagnosis. Children aged <28 days and those with severe acute malnutrition were excluded.

Results: The prevalence of dehydration in children without diarrhoea was 3.0% (2,019/68,204) and comprised 15.9% (2,019/12,702) of all dehydration cases. Only 55.8% (1,127/2,019) of affected children received either oral or intravenous fluid therapy. Where fluid treatment was given, the volumes, type of fluid, duration of fluid therapy, and route of administration were similar to those used in treatment of dehydration secondary to diarrhoea. Pneumonia (1021/2,019, 50.6%) and malaria (715/2,019, 35.4%) were the two most common co-morbid diagnoses. Overall case fatality in the study population was 12.9% (260/2,019).

Conclusion: Sixteen percent of children hospitalised with dehydration do not have diarrhoea but other common illnesses. Two-fifths do not receive fluid therapy, a regimen similar to that used in diarrhoeal cases is used in cases where fluid is administered. Efforts to promote compliance with guidance in routine clinical settings should recognise special circumstances where guidelines do not apply and further studies on appropriate management for dehydration in the absence of diarrhoea are required.

Keywords: Dehydration, Diarrhoea, Fluid management, Prevalence, Children, Kenya
**Article summary**

*Strengths of this study*

- Focuses broadly on dehydration from non-diarrhoeal causes where concerns of potential harm with fluid therapy remain.
- Data used is collected from routine practice across many hospitals rather than under research conditions therefore reflect real-world settings.
- Highlights that dehydration is common in children without diarrhoea but their treatment is similar to that used in diarrhoea and dehydration and there is no specific guidance for fluid therapy in non-diarrhoeal cases.

*Limitations of this study*

- Some treatment might have been documented but not given or administered but not documented.
- Use of registry data presenting possibility of ascertainment and selection biases.
BACKGROUND

Dehydration in children is commonly secondary to diarrhoea but other serious illnesses may also cause dehydration because of vomiting, reduced intake of fluids due to decreased appetite, increased insensible water loss due to fever, tachypnoea or compromised skin integrity. The World Health Organization (WHO) has guidelines for fluid therapy in children aged 1-59 months with diarrhoea and dehydration (DD) which involves use of isotonic intravenous fluids or oral rehydration therapy depending on severity of dehydration. (Table 1) Usually, liberal volumes which may include fluid boluses are recommended for the more severe forms of DD. However, cautious fluid therapy has been recommended in cases of non-diarrhoeal illnesses due to safety concerns and these fears have been supported by findings of the FEAST study. FEAST study was a large randomised controlled trial of alternative fluid management strategies for shock and impaired perfusion in febrile children in Africa, which showed use of fluid boluses to be harmful for treatment of shock or impaired perfusion in children without diarrhoea. The burden of dehydration in the absence of diarrhoea in admitted children and fluid management approach adopted by clinicians in such cases is unclear in the study setting. Conditions such as pneumonia, malaria, and meningitis are common causes of febrile illnesses, childhood admission, and mortality in Kenya and many resource-poor settings. These conditions may present with complications that may lead to dehydration even in the absence of diarrhoea where liberal fluid therapy may be harmful. In this study, we use routine data collected prospectively from 13 hospitals in Kenya to explore the prevalence of dehydration in the absence of diarrhoea, underlying diagnoses, fluid management practices, and case fatality for children aged 1-59 months admitted with dehydration but without diarrhoea.

METHODS

Study design and setting

This is a multi-site observational study that used routine in-patient data collected prospectively between October 2013 and December 2018. Data used in this study were collected from 13 hospitals involved in a collaborative effort, called the clinical information network (CIN), to monitor and promote uptake of recommended inpatient management guidelines. Five of the hospitals are located in western Kenya with high malaria transmission whereas the other eight are...
within central Kenya where there is no local transmission of malaria.\textsuperscript{16} Inception of the network, processes involved, and data quality assurance procedures have been described previously.\textsuperscript{15} 17 18 In brief, all clinical assessments and decisions on treatment are made by routine hospital staff. Upon discharge or death of a patient, data were abstracted from medical records in each hospital by trained data clerks guided by standardized operating procedures. Data were abstracted to a REDCap system – a non-proprietary data capture system-. The data clerks abstracted information on each patient’s clinical presentation, findings of physical examination, laboratory tests, admission diagnoses and treatment given from a standardized paediatric admission record, other medical notes, and treatment sheet. Information on discharge diagnosis and outcomes are obtained from standardised paediatric discharge summary that has also been adopted across CIN hospitals. Use of standardised forms and standardized operating procedures minimised information bias during data abstraction.

**Table 1: Guidelines for management of dehydration for children aged \( \geq 1 \) month (excluding severe malnutrition).**

| Classification          | Clinical Signs                                                                 | Recommended fluid management          |
|------------------------|--------------------------------------------------------------------------------|----------------------------------------|
| Shock                  | All of; Weak/absent pulse, altered consciousness AVPU<A, Temperature gradient (cold hands), capillary refill>3 seconds PLUS sunken eyes and slow skin pinch | Fluid bolus Ringer’s lactate/normal saline 20mls/kg |
| Severe Dehydration     | Two or more of; altered consciousness AVPU<A or lethargy, unable to drink, sunken eyes, return of skin pinch \( \geq 2 \) seconds | **PLAN C: STEP 1:** 30mls/kg Ringer’s lactate over 30minutes if age \( \geq 12 \) months OR over 1 hr if age < 12 months.  
**STEP 2:** 70mls/kg Ringer’s lactate over 2.5hours if age \( \geq 12 \) months OR over 5 hours if age < 12 months |
| Some Dehydration       | Two or more of; drinks eagerly, sunken eyes, restlessness or irritable, return of skin pinch 1-2 seconds | **PLAN B:** 75mls/kg ORS over 4hrs |
| No dehydration         | Less than 2 signs. Not enough to classify as some or severe dehydration          | **PLAN A:** 10mls/kg ORS after every loose stool |

Adapted from WHO Pocket book of hospital care for children: Guidelines for the management of common illnesses with limited resources (2nd Edition, 2013)\textsuperscript{2} and Kenya Basic Paediatric protocols(January 2016 Edition)\textsuperscript{3}
Study population

We analysed data for children aged 1-59 months collected between October 2013 and December 2018. We excluded 10 months of data from a period characterised by health workers strike between December 2016 to November 2017 because there was marked reduction in number of admissions.\(^\text{19}\) We also excluded neonates and those with severe acute malnutrition (SAM) defined as; mid-upper arm circumference (MUAC) <11.5cm for age \(\geq 6\) months, weight-for-height z-score (WHZ) of \(< -3\) standard deviations for children aged \(< 6\) months, or a clinical diagnosis of SAM. Those with SAM were excluded because they have different management guidelines and dehydration is difficult to diagnose clinically\(^\text{20}\) while for neonates, only minimal data(restricted to information on basic demographic characteristics, diagnoses and admission outcome that is required for routine national health information reporting) are collected and therefore detailed processes of care and admission characteristics could not be described. We also excluded data of non-medical cases including burns, and surgical cases that require specialised care.

The database was reviewed and those with a diagnosis of dehydration at admission or discharge but without diarrhoea as a diagnosis or presenting symptom at admission or discharge were identified. To confirm the absence of diarrhoea and rule out data entry errors, we retrieved a random sample list of patients identified from two hospitals located near Nairobi, where the researchers are based, and one investigator with a medical background visited the hospitals and reviewed the medical records. The records were checked for the presenting symptoms, assessment during admission, in-patient medical notes from the ward rounds, admission and discharge diagnoses, and the data were entered into a separate database. Data collected from medical records were linked using unique patient identifiers to the wider CIN database. We compared findings recorded from medical records review to those in the CIN database specifically for diagnosis or history of diarrhoea.

Data analysis

We described the characteristics of the study population using proportions for binary, categorical and nominal data, means (standard deviations) for normally distributed continuous data and medians (and interquartile ranges) for skewed or ordinal data. The proportion of children with dehydration diagnosis at admission or discharge but without diarrhoea was calculated overall and
for each hospital. We also described fluid management (fluid type, volumes, and duration), patient’s characteristics, and underlying diagnoses and case fatality.

**Ethical Considerations**

The CIN project and audit for routine care has been approved by the Kenya Medical Research Institute (KEMRI) Scientific and Ethics Review Unit (SERU) who have approved use of de-identified data for analysis and publication. Primary data belongs to respective hospitals. This work was supported by funds from Wellcome Trust but the funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Patient and Public Involvement**

This study was done without patient involvement. However, the Ministry of Health, county health executives, and all hospital management teams gave permission for this work to be developed and has supported the implementation of the CIN. The study findings have been disseminated to the hospital clinical teams in all the paediatric wards who provide care to the children for whom CIN project is designed.
RESULTS

Demographic characteristics of the study population

A total of 68,204 eligible children were admitted across the 13 study hospitals between October 2013 and December 2018. Figure 1 illustrates selection of the study population. The prevalence of dehydration in children without diarrhoea was 3.0% (2,019/68,204) (range 2.1%-4.3% across hospitals) and this comprised 15.9% (2,019/12,702) of all dehydration cases. Children admitted in hospitals located in areas with high malaria transmission accounted for 45.2% (912/2,019) of the study population. The median age was 14 months (interquartile range, 7-26 months). Sex was documented in 99% (2,001/2,019) of the population, 53.3% (1,067/2,001) of whom were male. More than half, 62.1% (1,254/2,019) were febrile (either had a history of fever or temperature $\geq 39^\circ C$ at admission), while 16.3% (329/2,019) had signs suggestive of impaired circulation shown by either weak pulse, capillary refill of $\geq 3$ seconds, temperature gradient or tachycardia (pulse rate $> 180$ beats per minute for children less than 12 months, $> 160$ beats per minute for those aged 12 months and above but below 60 months).

A total of 106 linked medical records were retrieved for validation from the two hospitals to ascertain the absence of diarrhoea diagnosis in recorded diagnosis or case notes. Review of the case notes showed that none had a diagnosis of diarrhoea or diarrhoea as symptom that may have been missed by the data clerk. Dehydration diagnosis without diarrhoea as recorded in the database and analysed here was therefore accurate.

Based on documented clinical diagnosis, some dehydration was the most common presentation (1,227/2,019, 60.8%), followed by severe dehydration (491/2,019, 24.3%), and shock was least common (142/2,019, 7.0%). Dehydration was not classified in 7.9% (159/2,019) of the cases. Characteristics of study participants are summarised in Table 2. The major clinical diagnoses in this population were pneumonia (50.6%, 1,021/2,019), malaria (35.4%, 715/2,019), anaemia (13.4%, 271/2,019), clinically diagnosed meningitis (11.9%, 241/2,019) and moderate malnutrition (10.5%, 212/2,019). Most patients 93.6% (1,881/2019) had comorbidities in addition to dehydration whereby a co-existence of malaria and pneumonia was the most common 248/2,019 (12.3%), followed by anaemia and malaria 182/2,019 (9.0%) as shown in Figure 2.
The overall case fatality was 12.9% (260/2019) and was directly related to the severity of dehydration-shock (50%, 71/142), severe dehydration (20.8%, 102/491), some dehydration (5.5%, 67/1,227). Case fatality for unclassified dehydration was 12.6% (20/159)

**Table 2. Characteristics of study participants**

| Population characteristics                          |  |
|-----------------------------------------------------|---|
| Age in months, median (interquartile range)         | 14(7-26) |
| Sex (male %)                                        | 1067/2001(53.3%) |
| Weight (Kg), mean±standard deviation                | 9.0±3.7 |
| MUAC (cm), median(interquartile range)              | 13.7(12.5-15.0) |

| Clinical characteristics                             | n/N (%) |
|-----------------------------------------------------|---------|
| Capillary refill >2seconds                           | 128/1287(10.0) |
| Sunken eyes                                         | 546/1464(37.3) |
| Delayed skin pinch                                  | 627/1489(42.1) |
| Weak pulse                                          | 193/1471(13.1) |
| History of Fever                                    | 1239/1614(76.7) |
| Temperature >= 39°C                                 | 240/1439(16.7) |
| Temperature Gradient                                | 132/1257(10.5) |
| Impaired consciousness                              | 193/1594(12.1) |
| Cannot drink/breastfeed                             | 431/1514(28.5) |
| History of vomiting                                 | 1058/1599(66.2) |
| Impaired perfusion                                  | 329/1,578(20.9) |
| Vomits everything                                   | 661/1002(66.0) |
| Age <1 year                                         | 819/2019(40.6) |
| Non-diarrhoeal dehydration/total dehydration       | 2019/12702(15.9) |

| Clinical Diagnosis                                  | n/N (%) |
|-----------------------------------------------------|---------|
| Pneumonia                                           | 1021/2019(50.6) |
| Malaria                                             | 715/2019(35.4) |
| Anaemia                                             | 271/2019(13.4) |
| Meningitis                                          | 241/2019(11.9) |
| Malnutrition                                        | 212/2019(10.5) |

| Case fatality                                       | n/N (%) |
|-----------------------------------------------------|---------|
| Shock                                               | 71/142(50.0) |
| Severe dehydration                                  | 102/491(20.8) |
| Some dehydration                                    | 67/1227(5.5) |
| Unclassified dehydration                            | 20/159(12.6) |
Fluid management practices

A total 55.8% (1,127/2,019) of children with dehydration had a fluid prescription either intravenous or oral - as summarised in Table 3. For those prescribed intravenous fluids, fluid bolus or Plan C was prescribed in 27.0% (545/2,019), while maintenance fluid was prescribed in 14.7% (296/2019) cases. Oral rehydration therapy (plans A or B) without intravenous fluids was prescribed in 17.8% (359/2,019) of cases. However, there were wide variations across hospitals in the use of intravenous fluids ranging from 22.1% to 55.4% or exclusive use of oral fluids, ranging from 7.2% to 38.7%. Nevertheless, use of intravenous fluid in general and fluid bolus were more common in children with severe forms of dehydration. However, notable cases with clinical signs of some dehydration received intravenous fluids, 33.1% (406/1,227), and a few received fluid boluses, 1.2% (15/1227).

In the febrile group, n=1254, 65.3 (819/1254) had a fluid prescribed. Intravenous fluids prescribed in 30% (376/1254) while oral fluid prescribed in 32.6% (409/1,254). Maintenance fluid was prescribed in 18.7% (234/1,254). Use of fluid bolus in this group was 3.6% (45/1,254).

Table 3. Fluid management

| Fluid Therapy | All Cases % (n/N) | Shock | Severe | Some | Not classified |
|---------------|------------------|-------|--------|------|---------------|
| Any fluid     | 55.8 (1127/2019) | 62.7  | 50.7   | 58.8 | 42.1          |
| IV fluid      | 27.0 (545/2019)  | 50.0  | 41.3   | 20.5 | 12.0          |
| Plan C        | 25.4 (513/2019)  | 38.0  | 40.3   | 19.7 | 12.0          |
| Fluid bolus   | 3.8 (77/2019)    | 31.0  | 3.7    | 1.2  | 0             |
| Maintenance fluid | 14.7 (296/2019) | 16.9  | 11.8   | 15.0 | 18.9          |
| Oral fluid    | 27.8 (562/2019)  | 9.2   | 16.9   | 35.8 | 17.0          |
| Plan A        | 10.2 (206/2019)  | 7.0   | 7.9    | 11.3 | 12.0          |
| Plan B        | 19.5 (394/2019)  | 2.8   | 9.2    | 26.8 | 10.1          |
| Both oral and IV | 10.1 (203/2019) | 4.9   | 13.7   | 10.2 | 3.7           |
| Oral fluid only | 17.8 (359/2019) | 4.2   | 3.3    | 25.8 | 13.2          |
| Maintenance fluid only | 0.6 (12/2019) | 0     | 0.2    | 0.7  | 1.3           |

Ringer’s lactate and normal saline were the most commonly used intravenous fluids for treatment of shock, (58/74, 78.4%) and (9/74, 12.2%). In participants with shock who had duration of fluid
bolus documented, 86.2% (25/29) received bolus fluid rapidly and the rest, 13.8% (4/29), received bolus over 1-2 hours. Median volume of fluid bolus was 20ml per kilogram body weight (interquartile range, 20-30ml). For treatment of severe dehydration, plan C was prescribed in 40.3% (198/491), both step one and two prescribed in 23.6% (116/491) cases. For those younger than 12 months, the median duration of fluid treatment was 6 hours (interquartile range 5-6 hours), while in children 1 year and above the median duration of fluid treatment was 3 hours (interquartile range 3-4 hours). The median volume given was 100ml/kilogram body weight (interquartile range 93-100 ml/kg). Plan B was used in 26.8% (329/1227) participants with some dehydration, median volume given was 75ml/kilogram body weight (interquartile range 74-75 ml/kg) and was given over a median duration of 4 hours (interquartile range 4-4 hours).

DISCUSSION

The study was conducted to estimate the prevalence of dehydration from non-diarrhoeal illnesses and establish fluid management practices used routinely by clinicians in the absence of clear guidance. This is the first study locally focusing broadly on dehydration from non-diarrhoeal causes since previous studies have concentrated on shock and impaired circulation which are often adverse effects of untreated dehydration or a consequence of severe sepsis.7 8 12 14 21 Our study is important especially after concerns generated following findings of the FEAST trial9 where fluid boluses, which are recommended for treatment of hypovolaemic shock secondary to diarrhoea,2 4 were shown to be harmful when used to treat shock in those with non-diarrhoeal illnesses. We therefore not only highlight the magnitude of a group of children who may need a different approach to fluid management but also those at risk of potentially harmful therapy.

Our study shows an overall low prevalence of dehydration in patients with non-diarrhoeal illnesses, but it still accounts for about 16% of all cases of dehydration, which is significant in a global context and important when considering children that may be exposed to potentially harmful treatment when liberal fluid therapy is used. Ascertainment through record linkage in two hospitals showed that these were not cases where diarrhoea was present as a symptom or diagnosis but missed at data entry. Fluid treatment, either oral or intravenous, is less frequently used to manage dehydration in the absence of diarrhoea, 55.8%(1,127/2,019) versus 78.2% (6,696/8,562) in
children with diarrhoea and dehydration (data not shown, previously described).\textsuperscript{22} However, where fluid treatments are given, the route of administration, fluid type, duration of administration and volumes were similar to those recommended in diarrhoea and dehydration. We found some discrepancy in the fluid regimen recorded in patients with various severities of dehydration. For example, there was use of fluid bolus in a child without shock, but we believe that this may be due to rapid change of clinical signs of dehydration. Such children without a diagnosis of shock who received fluid bolus could be those who initially presented with clinical signs of shock at the outpatient department, but the signs rapidly changed after fluid bolus is administered before assessment at the ward, where the characteristics captured in the database are recorded. Case fatality from dehydration in children with non-diarrhoeal illnesses (12.9%, 260/2,019) was also higher than that seen in patients with dehydration and diarrhoea previously.\textsuperscript{22, 23} Pneumonia and malaria were common underlying illnesses, and this has also been reported in previous studies.\textsuperscript{8, 12, 13, 24, 25}

Dehydration in patients without diarrhoea is not surprising because it may be caused by a number of mechanisms such as loss of fluids through vomiting, increased insensible losses from fever and due to high surface area to volume ratio in the under-fives who were the participants in this study.\textsuperscript{1} These mechanisms have been reported in malaria\textsuperscript{12-14} and pneumonia,\textsuperscript{8} which are the two major underlying diagnoses in this study. While less children received rehydration therapy compared to cases with diarrhoea and dehydration, use of similar fluid management approach to that of diarrhoea cases raises concerns of potential harm in malaria,\textsuperscript{9} pneumonia,\textsuperscript{7} and meningitis\textsuperscript{7, 26} especially when vascular changes leading to fluid redistribution in vasculature may also be at play. Although this study investigated dehydration rather than impaired circulation as was done in the FEAST study, we think the findings of the FEAST study may have some relevance to this population due to potential in change in condition in real world. Fluid bolus use resulted in increased mortality within the first 48 hours in children admitted with severe infection (57% of whom had malaria) and impaired perfusion in the FEAST study.\textsuperscript{9} Two well powered systematic reviews where the FEAST study was included, agreed with findings from the FEAST study.\textsuperscript{27, 28} Less frequent rehydration therapy in non-diarrhoea illnesses recorded in this study could be a result of cautious use of fluid therapy in non-diarrhoea illnesses such as pneumonia. The high case fatality could be due to underlying diagnoses and dehydration in these cases may be a marker of severity leading to increased risk of death. It is also possible that treatment is wrongly withheld,
or a wrong fluid treatment given being responsible for the higher case fatality, but this is only speculative. Fewer children with dehydration without diarrhoea received fluid therapy and it’s not clear if this decision is correct and fluid regimen to use in non-diarrhoeal cases is contentious. Nevertheless, these findings warrant further attention given the findings in the FEAST study and its significance to the study population. We have previously shown low use of fluid boluses in these hospitals,\textsuperscript{29} which is reassuring, but data analysed captured a period before widespread dissemination of the new WHO fluid guidelines\textsuperscript{4} and results in this study are reassuring.

Hospitals in this study receive regular feedback on care processes given to admitted children and the network also has data quality assurance procedures in place. We are therefore confident that the data is of good quality and this was reinforced by the validation from the file linkage in this study. CIN procedures have also improved documentation of assessment, diagnosis, classification, and treatments and this allows for the analysis presented here which may be difficult to repeat in settings without activities such as done within CIN.\textsuperscript{30} However, the findings are still generalisable because of diversity of hospitals involved and use of routine data rather than those collected under research conditions.

These results highlight varied practice in the absence of clear guidance for use by frontline clinicians in resource poor settings, who are often junior clinicians. We recognise that guidelines cannot cover all imaginable clinical scenarios, but fluid treatment is quite a common practice in hospitals and guidance for this group may be necessary. However, this will only be possible after definitive studies to address their fluid therapy given the concerns seen in the FEAST study.\textsuperscript{31} While these children did not have diarrhoea, even those with dehydration secondary to diarrhoea frequently present with other conditions where cautious fluid management is advised.\textsuperscript{22} Therefore, further studies may also be necessary to investigate appropriate fluid management for those with diarrhoea and dehydration complicated with other illnesses.

**Limitations**

Our study was limited in several ways; some treatment might have been documented but not given or administered but not documented and we can’t ascertain actual administration. Use of registry data is also known for its limitations with ascertainment and selection biases being persisting concerns. We also used clinician diagnoses without checking whether these reflected correct
diagnoses based on clinical signs and there can be misdiagnosis due to errors, clinical inexperience, and lack of adequate knowledge.\(^\text{32}\)

**CONCLUSION**

Sixteen percent of children hospitalised with dehydration do not have diarrhoea. Although dehydration is uncommon in children without diarrhoea, the case fatality is higher compared to that in children with diarrhoea. Clinicians are less likely to use fluids for treatment of dehydration when there is no diarrhoea, but they use same fluid regime like that for diarrhoeal cases when they prescribe fluid therapy, which is potentially harmful. Efforts to promote compliance with guidance in routine clinical settings should recognise special circumstances where guidelines do not apply and in need for further evidence.

**AUTHORS CONTRIBUTIONS AND COLLABORATORS.**

SA and ME conceptualised and designed the study with contribution from JA, DG and AA. SO collected case notes review data. SO analysed the data and drafted the initial manuscript with input from SA and other co-authors. All authors reviewed and provided input into the final version of the manuscript.

The Clinical Information Network author group who contributed to the network’s development, data collection, data management, implementation of audit and feedback includes: Grace Irimu, Morris Ogero, Mercy Chepkirui, George Mbevi, Cynthia Khazenzi at KEMRI Wellcome Trust Research Programme (KWTRP) developed the CIN approach and database tools. The CIN authors who contributed to the work, collection of data, and data quality assurance include: Victor Juma and Samuel Ng’arng’ar (Vihiga County Hospital); Boniface Nyumbile and Roselyne Malangachi (Kakamega County Hospital); Loice Mutai, Christine Manyasi, and David Kimutai (Mbagathi County Hospital); Caren Emadau, Atieno Jowi, Cecilia Mutiso and Celia Muturi (Mama Lucy Kibaki County Hospital); Charles Nzioki and Supa Tunje (Machakos County Hospital); Francis Kanyingi and Agnes Mithamo (Nyeri County Hospital); Magdalene Kuria (Kisumu East County Hospital); Sam Otido and Esther Mukami Njiru (Embu County Hospital); Peninah Muthoni and Peris Njiiri (Kerugoya County Hospital); Rachel Inginia and Melab Musabi
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The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

COMPETING INTERESTS

None

DATA SHARING STATEMENT

The source data are owned by the Kenyan Ministry of Health and County Governments. Users who wish to reuse the source data should make a request through the KEMRI-Wellcome Trust Research Programme data governance committee.

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**LEGENDS TO TABLES AND FIGURES**
Figure 1: Flow diagram showing patient selection.

Figure 2: Venn diagram showing sets of combinations of top 4 comorbidities in addition to dehydration. Other diagnoses not in top 4 are denoted by “Others”.

Table 1: Guidelines for management of dehydration for children aged ≥ 1 month (excluding severe malnutrition).

Table 2: Characteristics of study participants

Table 3: Fluid management
Figure 1: Flow diagram showing patient selection.
Figure 2: Venn diagram showing sets of combinations of top 4 comorbidities in addition to dehydration. Other diagnoses not in top 4 are denoted by "Others".

228x127mm (300 x 300 DPI)
The STROBE statement, that should be reported in observational studies.

| Item No. | STROBE items | Location in manuscript where items are reported |
|----------|--------------|-----------------------------------------------|
| **Title and Abstract** | 1 (a) Indicate the study’s design with a commonly used term in the title or the abstract | Title and Abstract: design sub-section |
| | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | Abstract: Design, Participants, Results sub-sections |
| **Introduction** | 2 Explain the scientific background and rationale for the investigation being reported | Background |
| **Objectives** | 3 State specific objectives, including any prespecified hypotheses | Background |
| **Methods** | 4 Present key elements of study design early in the paper | Methods: Study design and setting sub-section |
| **Setting** | 5 Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Methods: Study design and setting sub-section |
| **Participants** | 6 (a) Give the eligibility criteria, and the sources and methods of selection of participants | Methods: Study population subsection |
| **Variables** | 7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. | Not applicable |
| **Data sources/measurement** | 8 For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | Methods: Study design and setting |
| **Bias** | 9 Describe any efforts to address potential sources of bias | Methods: Study design and setting |
| **Study size** | 10 Explain how the study size was arrived at | Methods: Study population |

We used all records meeting inclusion criteria during the study period, hence no sampling required.
### Methods: Data analysis

| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | Methods: Data analysis |
|------------------------|----|------------------------------------------------------------------------------------------------------------------|------------------------|
| Statistical methods    | 12 | (a) Describe all statistical methods, including those used to control for confounding | Methods: Data analysis |
|                        |    | (b) Describe any methods used to examine subgroups and interactions | Not applicable |
|                        |    | (c) Explain how missing data were addressed | Not applicable |
|                        |    | (d) If applicable, describe analytical methods taking account of sampling strategy | Not applicable |
|                        |    | (e) Describe any sensitivity analyses | Not applicable |

### Results

#### Participants

| 13 | (a) Report the numbers of individuals at each stage of the study (e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) | Results: Figure 1 |
|    | (b) Give reasons for non-participation at each stage. | |
|    | (c) Consider use of a flow diagram | |

#### Descriptive data

| 14 | (a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders | Results: Demographic characteristics of the study population and Table 2 |
|    | (b) Indicate the number of participants with missing data for each variable of interest | |

#### Outcome data

| 15 | Report numbers of outcome events or summary measures | Results |

#### Main results

| 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included | Not applicable |
|    | (b) Report category boundaries when continuous variables were categorized | Results: Patients characteristics |
|    | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | Not applicable |
| Other analyses | 17 | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses | Not applicable |
|Discussion| |
| Key results | 18 | Summarise key results with reference to study objectives | Discussion paragraph 2 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Discussion: Limitations |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Discussion |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | Discussion paragraph 5 |
|Other Information| |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | Funding section |
**Prevalence and fluid management of dehydration in children without diarrhoea admitted to Kenyan hospitals: A multi-site observational study.**

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Prevalence and fluid management of dehydration in children without diarrhoea admitted to Kenyan hospitals: A multi-site observational study.

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ABSTRACT

Objectives: To examine the prevalence of dehydration without diarrhoea among admitted children aged 1-59 months and describe fluid management practices in such cases.

Design: A multi-site observational study that used routine in-patient data collected prospectively between October 2013 and December 2018.

Settings: Study conducted in 13 county referral hospitals in Kenya.

Participants: Children aged 1-59 months with admission or discharge diagnosis of dehydration but had no diarrhoea as a symptom or diagnosis. Children aged <28 days and those with severe acute malnutrition were excluded.

Results: The prevalence of dehydration in children without diarrhoea was 3.0% (2,019/68,204) and comprised 15.9% (2,019/12,702) of all dehydration cases. Only 55.8% (1,127/2,019) of affected children received either oral or intravenous fluid therapy. Where fluid treatment was given, the volumes, type of fluid, duration of fluid therapy, and route of administration were similar to those used in treatment of dehydration secondary to diarrhoea. Pneumonia (1021/2,019, 50.6%) and malaria (715/2,019, 35.4%) were the two most common co-morbid diagnoses. Overall case fatality in the study population was 12.9% (260/2,019).

Conclusion: Sixteen percent of children hospitalised with dehydration do not have diarrhoea but other common illnesses. Two-fifths do not receive fluid therapy, a regimen similar to that used in diarrhoeal cases is used in cases where fluid is administered. Efforts to promote compliance with guidance in routine clinical settings should recognise special circumstances where guidelines do not apply and further studies on appropriate management for dehydration in the absence of diarrhoea are required.

Keywords: Dehydration, Diarrhoea, Fluid management, Prevalence, Children, Kenya
Article summary

Strengths of this study

- Focuses broadly on dehydration from non-diarrhoeal causes where concerns of potential harm with fluid therapy remain.
- Used routine data across many hospitals therefore reflects real-world settings.
- Highlights that though dehydration is common in children without diarrhoea, there is in no specific guidance for fluid therapy in non-diarrhoeal cases.

Limitations of this study

- Some treatment might have been documented but not given or administered but not documented.
- Use of registry data presenting possibility of ascertainment and selection biases.
BACKGROUND

Dehydration in children is commonly secondary to diarrhoea but other serious illnesses may also cause dehydration because of vomiting, reduced intake of fluids due to decreased appetite, increased insensible water loss due to fever, tachypnoea or compromised skin integrity.1 The World Health Organization (WHO) has guidelines for fluid therapy in children aged 1-59 months with diarrhoea and dehydration (DD) which involves use of isotonic intravenous fluids or oral rehydration therapy depending on severity of dehydration.2-5 (Table 1) Usually, liberal volumes which may include fluid boluses are recommended for the more severe forms of DD. However, cautious fluid therapy has been recommended in cases of non-diarrhoeal illnesses due to safety concerns6-8 and these fears have been supported by findings of the FEAST study. FEAST study was a large randomised controlled trial of alternative fluid management strategies for shock and impaired perfusion in febrile children in Africa,4 9 which showed use of fluid boluses to be harmful for treatment of shock or impaired perfusion in children without diarrhoea. The burden of dehydration in the absence of diarrhoea in admitted children and fluid management approach adopted by clinicians in such cases is unclear in the study setting. Conditions such as pneumonia, malaria, and meningitis are common causes of febrile illnesses, childhood admission, and mortality in Kenya and many resource-poor settings.10 These conditions may present with complications that may lead to dehydration even in the absence of diarrhoea where liberal fluid therapy may be harmful.11-14

In this study, we use routine data collected prospectively from 13 hospitals in Kenya15 to explore the prevalence of dehydration in the absence of diarrhoea, underlying diagnoses, fluid management practices, and case fatality for children aged 1-59 months admitted with dehydration but without diarrhoea.

METHODS

Study design and setting

This is a multi-site observational study that used routine in-patient data collected prospectively between October 2013 and December 2018. Data used in this study were collected from 13 hospitals involved in a collaborative effort, called the clinical information network (CIN), to monitor and promote uptake of recommended inpatient management guidelines. Five of the
hospitals are located in western Kenya with high malaria transmission whereas the other eight are within central Kenya where there is no local transmission of malaria. Inception of the network, processes involved, and data quality assurance procedures have been described previously. In brief, all clinical assessments and decisions on treatment are made by routine hospital staff. Upon discharge or death of a patient, data were abstracted from medical records in each hospital by trained data clerks guided by standardized operating procedures. Data were abstracted to a REDCap system – a non-proprietary data capture system-. The data clerks abstracted information on each patient’s clinical presentation, findings of physical examination, laboratory tests, admission diagnoses and treatment given from a standardized paediatric admission record, other medical notes, and treatment sheet. Information on discharge diagnosis and outcomes are obtained from standardised paediatric discharge summary that has also been adopted across CIN hospitals. Use of standardised forms and standardized operating procedures minimised information bias during data abstraction.

Table 1: Guidelines for management of dehydration for children aged ≥ 1 month (excluding severe malnutrition).

| Classification          | Clinical Signs                                                                 | Recommended fluid management                                      |
|-------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------|
| **Shock**               | All of; Weak/absent pulse, altered consciousness AVPU<A, Temperature gradient (cold hands), capillary refill>3 seconds PLUS sunken eyes and slow skin pinch | Fluid bolus Ringer's lactate/normal saline 20mls/kg                |
| **Severe Dehydration**  | Two or more of; altered consciousness AVPU<A or lethargy, unable to drink, sunken eyes, return of skin pinch ≥2 seconds | **PLAN C: STEP 1:** 30mls/kg Ringer’s lactate over 30 minutes if age ≥ 12 months OR over 1 hr if aged < 12 months. **STEP 2:** 70mls/kg Ringer’s lactate over 2.5 hours if age ≥ 12 months OR over 5 hours if age < 12 months |
| **Some Dehydration**    | Two or more of; drinks eagerly, sunken eyes, restlessness or irritable, return of skin pinch 1-2 seconds                  | **PLAN B:** 75mls/kg ORS over 4 hrs                                 |
| **No dehydration**     | Less than 2 signs. Not enough to classify as some or severe dehydration      | **PLAN A:** 10mls/kg ORS after every loose stool                   |

Adapted from WHO Pocket book of hospital care for children: Guidelines for the management of common illnesses with limited resources (2nd Edition, 2013) and Kenya Basic Paediatric protocols (January 2016 Edition).
Study population

We analysed data for children aged 1-59 months collected between October 2013 and December 2018. We excluded 10 months of data from a period characterised by health workers strike between December 2016 to November 2017 because there was marked reduction in number of admissions. We also excluded neonates and those with severe acute malnutrition (SAM) defined as: mid-upper arm circumference (MUAC) <11.5cm for age ≥6 months, weight-for-height z-score (WHZ) of < -3 standard deviations for children aged <6 months, or a clinical diagnosis of SAM. Those with SAM were excluded because they have different management guidelines and dehydration is difficult to diagnose clinically while for neonates, only minimal data restricted to information on basic demographic characteristics, diagnoses and admission outcome that is required for routine national health information reporting are collected and therefore detailed processes of care and admission characteristics could not be described. We also excluded data of non-medical cases including burns, and surgical cases that require specialised care.

The database was reviewed and those with a diagnosis of dehydration at admission or discharge but without diarrhoea as a diagnosis or presenting symptom at admission or discharge were identified. To confirm the absence of diarrhoea and rule out data entry errors, we retrieved a random sample list of patients identified from two hospitals located near Nairobi, where the researchers are based, and one investigator with a medical background visited the hospitals and reviewed the medical records. The records were checked for the presenting symptoms, assessment during admission, in-patient medical notes from the ward rounds, admission and discharge diagnoses, and the data were entered into a separate database. Data collected from medical records were linked using unique patient identifiers to the wider CIN database. We compared findings recorded from medical records review to those in the CIN database specifically for diagnosis or history of diarrhoea.

Data analysis

We described the characteristics of the study population using proportions for binary, categorical and nominal data, means (standard deviations) for normally distributed continuous data and medians (and interquartile ranges) for skewed or ordinal data. The proportion of children with
dehydration diagnosis at admission or discharge but without diarrhoea was calculated overall and for each hospital. We also described fluid management practices (fluid type, volumes, and duration), patient’s characteristics, and underlying diagnoses and case fatality.

**Ethical Considerations**

The CIN project and audit for routine care has been approved by the Kenya Medical Research Institute (KEMRI) Scientific and Ethics Review Unit (SERU) who have approved use of de-identified data for analysis and publication. Primary data belongs to respective hospitals. This work was supported by funds from Wellcome Trust but the funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Patient and Public Involvement**

This study was done without patient involvement. However, the Ministry of Health, county health executives, and all hospital management teams gave permission for this work to be developed and has supported the implementation of the CIN. The study findings have been disseminated to the hospital clinical teams in all the paediatric wards who provide care to the children for whom CIN project is designed.
RESULTS

Demographic characteristics of the study population

A total of 68,204 eligible children were admitted across the 13 study hospitals between October 2013 and December 2018. Figure 1 illustrates selection of the study population. The prevalence of dehydration in children without diarrhoea was 3.0% (2,019/68,204) (range 2.1%-4.3% across hospitals) and this comprised 15.9% (2,019/12,702) of all dehydration cases. Children admitted in hospitals located in areas with high malaria transmission accounted for 45.2% (912/2,019) of the study population. The median age was 14 months (interquartile range,7-26 months). Sex was documented in 99.0% (2,001/2,019) of the population, 53.3% (1,067/2,001) of whom were male. More than half, 62.1% (1,254/2,019) were febrile (either had a history of fever or temperature \( \geq 39^\circ\text{C} \) at admission), while 16.3% (329/2,019) had signs suggestive of impaired circulation shown by either weak pulse, capillary refill of \( \geq 3 \) seconds, temperature gradient or tachycardia (pulse rate \( >180 \) beats per minute for children less than 12 months, \( >160 \) beats per minute for those aged 12 months and above but below 60 months).

A total of 106 linked medical records were retrieved for validation from the two hospitals to ascertain the absence of diarrhoea diagnosis in recorded diagnosis or case notes. Review of the case notes showed that none had a diagnosis of diarrhoea or diarrhoea as symptom that may have been missed by the data clerk. Dehydration diagnosis without diarrhoea as recorded in the database and analysed here was therefore accurate.

Based on documented clinical diagnosis, some dehydration was the most common presentation (1,227/2,019, 60.8%), followed by severe dehydration (491/2,019, 24.3%), and shock was least common (142/2,019, 7.0%). Dehydration was not classified in 7.9% (159/2,019) of the cases. Characteristics of study participants are summarised in Table 2. The major clinical diagnoses in this population were pneumonia (50.6%, 1,021/2,019), malaria (35.4%, 715/2,019), anaemia (13.4%, 271/2,019), clinically diagnosed meningitis (11.9%, 241/2,019) and moderate malnutrition (10.5%, 212/2,019). Most patients 93.6% (1,881/2019) had comorbidities in addition to dehydration whereby a co-existence of malaria and pneumonia was the most common 248/2,019 (12.3%), followed by anaemia and malaria 182/2,019(9.0%) as shown in Figure 2.
The overall case fatality was 12.9% (260/2019) and was directly related to the severity of dehydration-shock (50.0%, 71/142), severe dehydration (20.8%, 102/491), some dehydration (5.5%, 67/1,227). Case fatality for unclassified dehydration was 12.6% (20/159).

Case fatality was 134 (11.9%) in children where prescribed any fluid compared to 126 (14.1%) in those without any fluid prescribed. The case fatalities were 125 (16.3%) and 135 (10.8%) respectively in patients prescribed intravenous fluids versus those without intravenous fluids prescriptions. Case fatality was lowest in children prescribed only oral fluids, 9 (2.5%) and moderate for those with oral plus intravenous fluid prescriptions, 15 (7.4%).
Table 2. Characteristics of study participants

| Population characteristics |  
|-----------------------------|
| Age in months, median (interquartile range) | 14(7-26)  
| Sex (male %) | 1067/2001(53.3%)  
| Weight (Kg), mean±standard deviation | 9.0±3.7  
| MUAC (cm), median(interquartile range) | 13.7(12.5-15.0)  

| Clinical characteristics | n/N* (%)  
|--------------------------|
| Capillary refill >2seconds | 128/1287(10.0)  
| Sunken eyes | 546/1464(37.3)  
| Delayed skin pinch | 627/1489(42.1)  
| Weak pulse | 193/1471(13.1)  
| History of Fever | 1239/1614(76.7)  
| Temperature >= 39°C | 240/1439(16.7)  
| Temperature Gradient | 132/1257(10.5)  
| Impaired consciousness | 193/1594(12.1)  
| Cannot drink/breastfeed | 431/1514(28.5)  
| History of vomiting | 1058/1599(66.2)  
| Impaired perfusion | 329/1,578(20.9)  
| Vomits everything | 661/1002(66.0)  
| Age <1 year | 819/2019(40.6)  
| Non-diarrhoeal dehydration/total dehydration | 2019/12702(15.9)  

| Clinical Diagnosis | N=2019,n (%)  
|--------------------|
| Pneumonia | 1021 (50.6)  
| Malaria | 715 (35.4)  
| Anaemia | 271 (13.4)  
| Meningitis | 241 (11.9)  
| Malnutrition | 212 (10.5)  

| Case fatality | n/N (%)  
|---------------|
| Shock | 71/142(50.0)  
| Severe dehydration | 102/491(20.8)  
| Some dehydration | 67/1227(5.5)  
| Unclassified dehydration | 20/159 (12.6)  

* denotes the study population was 2019, however the denominator for the patients’ characteristics varied based on documentation
Fluid management practices

A total 55.8% (1,127/2,019) of children with dehydration had a fluid prescription either intravenous or oral—as summarised in Table 3. For those prescribed intravenous fluids, fluid bolus was prescribed in 3.8% (77/2,019), while maintenance fluid was prescribed in 14.7% (296/2,019) cases. Oral rehydration therapy (plans A or B) without intravenous fluids was prescribed in 17.8% (359/2,019) of cases. However, there were wide variations across hospitals in the use of intravenous fluids ranging from 22.1% to 55.4% or exclusive use of oral fluids, ranging from 7.2% to 38.7%. Nevertheless, use of intravenous fluid in general and fluid bolus were more common in children with severe forms of dehydration. However, notable cases with clinical signs of some dehydration received intravenous fluids, 33.1% (406/1,227), and a few received fluid boluses, 1.2% (15/1,227).

In the febrile group, n=1,254, 65.3% (819/1,254) had a fluid prescribed. Intravenous fluids prescribed in 44.4% (557/1,254) while oral fluid prescribed in 32.6% (409/1,254). Maintenance fluid was prescribed in 18.7% (234/1,254). Use of fluid bolus in this group was 3.6% (45/1,254). Ringer’s lactate and normal saline were the most commonly used intravenous fluids for treatment of shock, (58/74, 78.4%) and (9/74, 12.2%). In participants with shock who had duration of fluid bolus documented, 86.2% (25/29) received bolus fluid rapidly and the rest, 13.8% (4/29), received bolus over 1-2 hours. Median volume of fluid bolus was 20ml per kilogram body weight (interquartile range, 20-30ml). For treatment of severe dehydration, plan C was prescribed in 40.3% (198/491), both step one and two prescribed in 23.6% (116/491) cases. For those younger than 12 months, the median duration of fluid treatment was 6 hours (interquartile range 5-6 hours), while in children 1 year and above the median duration of fluid treatment was 3 hours (interquartile range 3-4 hours). The median volume given was 100ml/kilogram body weight (interquartile range 93-100 ml/kg). Plan B was used in 26.8% (329/1,227) participants with some dehydration, median volume given was 75ml/kilogram body weight (interquartile range 74-75 ml/kg) and was given over a median duration of 4 hours (interquartile range 4-4 hours).
### Table 3. Fluid management

| Fluid Therapy | All Cases (N=2019), n (%) | Shock N=142, n (%) | Severe N=491, n (%) | Some N=1227, n (%) | Not classified N=159, n (%) |
|---------------|---------------------------|-------------------|---------------------|------------------|---------------------------|
| Any fluid     | 1127(55.8)                | 89(62.7)          | 249(50.7)           | 722(58.8)        | 67(42.1)                  |
| IV fluid      | 768(38.0)                 | 83(58.5)          | 233(47.5)           | 406(33.1)        | 46(28.9)                  |
| Plan C        | 513(25.4)                 | 54(38.0)          | 198(40.3)           | 242(19.7)        | 19(12.0)                  |
| Fluid bolus   | 77(3.8)                   | 44(31.0)          | 18(3.7)             | 15(1.2)          | 0.0                       |
| Maintenance fluid | 296(14.7)           | 24(16.9)          | 58(11.8)            | 184(15.0)        | 30(18.9)                  |
| Oral fluid    | 562(27.8)                 | 13(9.2)           | 83(16.9)            | 439(35.8)        | 27(17.0)                  |
| Plan A        | 206(10.2)                 | 10(7.0)           | 39(7.9)             | 138(11.3)        | 19(12.0)                  |
| Plan B        | 394(19.5)                 | 4(2.8)            | 45(9.2)             | 329(26.8)        | 16(10.1)                  |
| Both oral and IV | 203(10.1)             | 7(4.9)            | 67(13.7)            | 123(10.0)        | 6(3.8)                    |
| Oral fluid only | 359(17.8)              | 6(4.2)            | 16(3.3)             | 316(25.8)        | 21(13.2)                  |
| Maintenance fluid only | 12(0.6)            | 0.0               | 1(0.2)              | 9(0.7)           | 2(1.3)                    |
DISCUSSION

The study was conducted to estimate the prevalence of dehydration from non-diarrhoeal illnesses and establish fluid management practices used routinely by clinicians in the absence of clear guidance. This is the first study locally focusing broadly on dehydration from non-diarrhoeal causes since previous studies have concentrated on shock and impaired circulation which are often adverse effects of untreated dehydration or a consequence of severe sepsis.7 8 12 14 22 Our study is important especially after concerns generated following findings of the FEAST trial9 where fluid boluses, which are recommended for treatment of hypovolaemic shock secondary to diarrhoea,2 4 were shown to be harmful when used to treat shock in those with non-diarrhoeal illnesses. We therefore not only highlight the magnitude of a group of children who may need a different approach to fluid management but also those at risk of potentially harmful therapy.

Our study shows an overall low prevalence of dehydration in patients with non-diarrhoeal illnesses, but it still accounts for about 16% of all cases of dehydration, which is significant in a global context and important when considering children that may be exposed to potentially harmful treatment when liberal fluid therapy is used. Ascertainment through record linkage in two hospitals showed that these were not cases where diarrhoea was present as a symptom or diagnosis but missed at data entry. Fluid treatment, either oral or intravenous, is less frequently used to manage dehydration in the absence of diarrhoea, 55.8%(1,127/2,019) versus 78.2% (6,696/8,562) in children with diarrhoea and dehydration (data not shown, previously described).23 However, where fluid treatments are given, the route of administration, fluid type, duration of administration and volumes were similar to those recommended in diarrhoea and dehydration. We found some discrepancy in the fluid regimen recorded in patients with various severities of dehydration. For example, there was use of fluid bolus in a child without shock, but we believe that this may be due to rapid change of clinical signs of dehydration. Such children without a diagnosis of shock who received fluid bolus could be those who initially presented with clinical signs of shock at the outpatient department, but the signs rapidly changed after fluid bolus is administered before assessment at the ward, where the characteristics captured in the database are recorded. Case fatality from dehydration in children with non-diarrhoeal illnesses (12.9%, 260/2,019) was also higher than that seen in patients with dehydration and diarrhoea previously.23 24 Pneumonia and
malaria were common underlying illnesses, and this has also been reported in previous studies.\textsuperscript{8, 12} 13 25 26

Dehydration in patients without diarrhoea is not surprising because it may be caused by a number of mechanisms such as loss of fluids through vomiting, increased insensible losses from fever and due to high surface area to volume ratio in the under-fives who were the participants in this study.\textsuperscript{1} These mechanisms have been reported in malaria\textsuperscript{12-14} and pneumonia,\textsuperscript{8} which are the two major underlying diagnoses in this study. While less children received rehydration therapy compared to cases with diarrhoea and dehydration, use of similar fluid management approach to that of diarrhoea cases raises concerns of potential harm in malaria,\textsuperscript{9} pneumonia,\textsuperscript{7} and meningitis\textsuperscript{7, 27} especially when vascular changes leading to fluid redistribution in vasculature may also be at play. Although this study investigated dehydration rather than impaired circulation as was done in the FEAST study, we think the findings of the FEAST study may have some relevance to this population due to potential in change in condition in real world. Fluid bolus use resulted in increased mortality within the first 48 hours in children admitted with severe infection (57\% of whom had malaria) and impaired perfusion in the FEAST study.\textsuperscript{9} Two well powered systematic reviews where the FEAST study was included, agreed with findings from the FEAST study.\textsuperscript{28, 29}

Less frequent rehydration therapy in non-diarrhoea illnesses recorded in this study could be a result of cautious use of fluid therapy in non-diarrhoea illnesses such as pneumonia. The high case fatality could be due to underlying diagnoses and dehydration in these cases may be a marker of severity leading to increased risk of death. It is also possible that treatment is wrongly withheld, or a wrong fluid treatment given being responsible for the higher case fatality, but this is only speculative. Fewer children with dehydration without diarrhoea received fluid therapy and it’s not clear if this decision is correct and fluid regimen to use in non-diarrhoeal cases is contentious. Nevertheless, these findings warrant further attention given the findings in the FEAST study and its significance to the study population. We have previously shown low use of fluid boluses in these hospitals,\textsuperscript{30} which is reassuring, but data analysed captured a period before widespread dissemination of the new WHO fluid guidelines\textsuperscript{4} and results in this study are reassuring.

Hospitals in this study receive regular feedback on care processes given to admitted children and the network also has data quality assurance procedures in place. We are therefore confident that the data is of good quality and this was reinforced by the validation from the file linkage in this
study. CIN procedures have also improved documentation of assessment, diagnosis, classification, and treatments and this allows for the analysis presented here which may be difficult to repeat in settings without activities such as done within CIN. However, the findings are still generalisable because of diversity of hospitals involved and use of routine data rather than those collected under research conditions.

These results highlight varied practice in the absence of clear guidance for use by frontline clinicians in resource poor settings, who are often junior clinicians. We recognise that guidelines cannot cover all imaginable clinical scenarios, but fluid treatment is quite a common practice in hospitals and guidance for this group may be necessary. However, this will only be possible after definitive studies to address their fluid therapy given the concerns seen in the FEAST study. While these children did not have diarrhoea, even those with dehydration secondary to diarrhoea frequently present with other conditions where cautious fluid management is advised. Therefore, further studies may also be necessary to investigate appropriate fluid management for those with diarrhoea and dehydration complicated with other illnesses.

Limitations

Our study was limited in several ways; some treatment might have been documented but not given or administered but not documented and we can’t ascertain actual administration. Use of registry data is also known for its limitations with ascertainment and selection biases being persisting concerns. We also used clinician diagnoses without checking whether these reflected correct diagnoses based on clinical signs and there can be misdiagnosis due to errors, clinical inexperience, and lack of adequate knowledge.

CONCLUSION

Sixteen percent of children hospitalised with dehydration do not have diarrhoea. Although dehydration is uncommon in children without diarrhoea, the case fatality is higher compared to that in children with diarrhoea. Clinicians are less likely to use fluids for treatment of dehydration when there is no diarrhoea, but they use same fluid regime like that for diarrhoeal cases when they prescribe fluid therapy, which is potentially harmful. Efforts to promote compliance with guidance
in routine clinical settings should recognise special circumstances where guidelines do not apply and in need for further evidence.

AUTHORS CONTRIBUTIONS AND COLLABORATORS.

SA and ME conceptualised and designed the study with contribution from JA, DG and AA. SO collected case notes review data. SO analysed the data and drafted the initial manuscript with input from SA and other co-authors. All authors reviewed and provided input into the final version of the manuscript.

The Clinical Information Network author group who contributed to the network’s development, data collection, data management, implementation of audit and feedback includes: Grace Irimu, Morris Ogero, Mercy Chepkirui, George Mbevi, Cynthia Khazenzi at KEMRI Wellcome Trust Research Programme (KWTRP) developed the CIN approach and database tools. The CIN authors who contributed to the conduct of the work, collection of data, and data quality assurance include: Victor Juma and Samuel Ng’arng’ar (Vihiga County Hospital); Boniface Nyumbile and Roselyne Malangachi (Kakamega County Hospital); Loice Mutai, Christine Manyasi, and David Kimutai (Mbagathi County Hospital); Caren Emadau, Atieno Jowi, Cecilia Mutiso and Celia Muturi (Mama Lucy Kibaki County Hospital); Charles Nzioki and Supa Tunje (Machakos County Hospital); Francis Kanyangi and Agnes Mithamo (Nyeri County Hospital); Magdalene Kuria (Kisumu East County Hospital); Sam Otido and Esther Mukami Njiru (Embu County Hospital); Peninah Muthoni and Peris Njiiri (Kerugoya County Hospital); Rachel Inginia and Melab Musabi (Kitale County Hospital); Emma Sarah Namulala (Busia County Hospital); Grace Akech and Lydia Thuranira (Kiambu County Hospital);

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COMPETING INTERESTS

None

DATA SHARING STATEMENT

The source data are owned by the Kenyan Ministry of Health and County Governments. Users who wish to reuse the source data should make a request through the KEMRI-Wellcome Trust Research Programme data governance committee.

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**LEGENDS TO TABLES AND FIGURES**

Figure 1: Flow diagram showing patient selection.

Figure 2: Venn diagram showing sets of combinations of top 4 comorbidities in addition to dehydration. Other diagnoses not in top 4 are denoted by “Others”.

Table 1: Guidelines for management of dehydration for children aged ≥1 month (excluding severe malnutrition).

Table 2: Characteristics of study participants
Table 3: Fluid management
Figure 1: Flow diagram showing patient selection.
Figure 2: Venn diagram showing sets of combinations of top 4 comorbidities in addition to dehydration. Other diagnoses not in top 4 are denoted by "Others".

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The STROBE statement, that should be reported in observational studies.

| Item No. | STROBE items | Location in manuscript where items are reported |
|----------|--------------|-----------------------------------------------|
| Title and Abstract | 1 | (a) Indicate the study’s design with a commonly used term in the title or the abstract | Page 1, Title and page 2, paragraph 2. |
| | | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | Page 2, paragraph 1 to 5 |
| Introduction | 2 | Explain the scientific background and rationale for the investigation being reported | Page 4, paragraph 1 |
| | 3 | State specific objectives, including any prespecified hypotheses | Page 4, paragraph 2 |
| Methods | 4 | Present key elements of study design early in the paper | Page 4, paragraph 3; to page 5 Methods: Study design and setting sub-section |
| | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Page 4, paragraph 3; to page 5 Methods: Study design and setting sub-section |
| | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants | Page 6, paragraph 1 and 2 Methods: Study population subsection |
| | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. | Not applicable |
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| | | | Not applicable |
| | 9 | Describe any efforts to address potential sources of bias | Page 5, paragraph 1 Methods: Study design and setting Addresses efforts to minimise information bias. |
| Study size | 10 | Explain how the study size was arrived at | Page 6, paragraph 1 & 2 Methods: Study population We used all records meeting inclusion criteria during the study period, hence no sampling required |
|---|---|---|---|
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | Page 6, paragraph 3 and page 7 paragraph 1 Methods: Data analysis |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses | Not applicable |
| Results | | (a) Report the numbers of individuals at each stage of the study (e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed) (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram | File upload 3: Study population flow chart. |
| Participants | 13 | (a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders (b) Indicate the number of participants with missing data for each variable of interest | Page 8 to page 10 Results: Demographic characteristics of the study population and Table 2 |
| Descriptive data | 14 | | |
| Outcome data | 15 | Report numbers of outcome events or summary measures | Page 11 to page 12 |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which | Not applicable |
| Section          | Page No. | Details                                                                                                                                                                                                 |
|------------------|----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Other analyses   | 17       | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses                                                                                                       |
| Discussion       |          |                                                                                                                                            |
| Key results      | 18       | Summarise key results with reference to study objectives                                                                                     |
| Limitations      | 19       | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                                                      |
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| Generalisability | 21       | Discuss the generalisability (external validity) of the study results                                                                         |
| Other Information|          |                                                                                                                                            |
| Funding          | 22       | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based                                                 |
Prevalence and fluid management of dehydration in children without diarrhoea admitted to Kenyan hospitals: A multi-site observational study.

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Prevalence and fluid management of dehydration in children without diarrhoea admitted to Kenyan hospitals: A multi-site observational study.

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ABSTRACT

Objectives: To examine the prevalence of dehydration without diarrhoea among admitted children aged 1-59 months and describe fluid management practices in such cases.

Design: A multi-site observational study that used routine in-patient data collected prospectively between October 2013 and December 2018.

Settings: Study conducted in 13 county referral hospitals in Kenya.

Participants: Children aged 1-59 months with admission or discharge diagnosis of dehydration but had no diarrhoea as a symptom or diagnosis. Children aged <28 days and those with severe acute malnutrition were excluded.

Results: The prevalence of dehydration in children without diarrhoea was 3.0% (2,019/68,204) and comprised 15.9% (2,019/12,702) of all dehydration cases. Only 55.8% (1,127/2,019) of affected children received either oral or intravenous fluid therapy. Where fluid treatment was given, the volumes, type of fluid, duration of fluid therapy, and route of administration were similar to those used in treatment of dehydration secondary to diarrhoea. Pneumonia (1021/2,019, 50.6%) and malaria (715/2,019, 35.4%) were the two most common co-morbid diagnoses. Overall case fatality in the study population was 12.9% (260/2,019).

Conclusion: Sixteen percent of children hospitalised with dehydration do not have diarrhoea but other common illnesses. Two-fifths do not receive fluid therapy, a regimen similar to that used in diarrhoeal cases is used in cases where fluid is administered. Efforts to promote compliance with guidance in routine clinical settings should recognise special circumstances where guidelines do not apply and further studies on appropriate management for dehydration in the absence of diarrhoea are required.

Keywords: Dehydration, Diarrhoea, Fluid management, Prevalence, Children, Kenya
Article summary

Strengths of this study

- Focuses broadly on dehydration from non-diarrhoeal causes where concerns of potential harm with fluid therapy remain.
- Used routine data across many hospitals therefore reflects real-world settings.
- Highlights that though dehydration is common in children without diarrhoea, there is in no specific guidance for fluid therapy in non-diarrhoeal cases.

Limitations of this study

- Some treatment might have been documented but not given or administered but not documented.
- Use of registry data presenting possibility of ascertainment and selection biases.
BACKGROUND

Dehydration in children is commonly secondary to diarrhoea but other serious illnesses may also cause dehydration because of vomiting, reduced intake of fluids due to decreased appetite, increased insensible water loss due to fever, tachypnoea or compromised skin integrity.\(^1\) The World Health Organization (WHO) has guidelines for fluid therapy in children aged 1-59 months with diarrhoea and dehydration (DD) which involves use of isotonic intravenous fluids or oral rehydration therapy depending on severity of dehydration.\(^2-5\) (Table 1) Usually, liberal volumes which may include fluid boluses are recommended for the more severe forms of DD. However, cautious fluid therapy has been recommended in cases of non-diarrhoeal illnesses due to safety concerns\(^6-8\) and these fears have been supported by findings of the FEAST study. FEAST study was a large randomised controlled trial of alternative fluid management strategies for shock and impaired perfusion in febrile children in Africa,\(^4,9\) which showed use of fluid boluses to be harmful for treatment of shock or impaired perfusion in children without diarrhoea. The burden of dehydration in the absence of diarrhoea in admitted children and fluid management approach adopted by clinicians in such cases is unclear in the study setting. Conditions such as pneumonia, malaria, and meningitis are common causes of febrile illnesses, childhood admission, and mortality in Kenya and many resource-poor settings.\(^10\) These conditions may present with complications that may lead to dehydration even in the absence of diarrhoea where liberal fluid therapy may be harmful.\(^11-14\)

In this study, we use routine data collected prospectively from 13 hospitals in Kenya\(^15\) to explore the prevalence of dehydration in the absence of diarrhoea, underlying diagnoses, fluid management practices, and case fatality for children aged 1-59 months admitted with dehydration but without diarrhoea.

METHODS

Study design and setting

This is a multi-site observational study that used routine in-patient data collected prospectively between October 2013 and December 2018. Data used in this study were collected from 13 hospitals involved in a collaborative effort, called the clinical information network (CIN), to monitor and promote uptake of recommended inpatient management guidelines. Five of the
hospitals are located in western Kenya with high malaria transmission whereas the other eight are within central Kenya where there is no local transmission of malaria. Inception of the network, processes involved, and data quality assurance procedures have been described previously. In brief, all clinical assessments and decisions on treatment are made by routine hospital staff. Upon discharge or death of a patient, data were abstracted from medical records in each hospital by trained data clerks guided by standardized operating procedures. Data were abstracted to a REDCap system – a non-proprietary data capture system-. The data clerks abstracted information on each patient’s clinical presentation, findings of physical examination, laboratory tests, admission diagnoses and treatment given from a standardized paediatric admission record, other medical notes, and treatment sheet. Information on discharge diagnosis and outcomes are obtained from standardised paediatric discharge summary that has also been adopted across CIN hospitals. Use of standardised forms and standardized operating procedures minimised information bias during data abstraction.

Table 1: Guidelines for management of dehydration for children aged ≥ 1 month (excluding severe malnutrition).

| Classification       | Clinical Signs                                                                                                                  | Recommended fluid management                                           |
|----------------------|----------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Shock                | All of; Weak/absent pulse, altered consciousness AVPU*<A, Temperature gradient (cold hands), capillary refill>3 seconds PLUS sunken eyes and slow skin pinch | Fluid bolus Ringer’s lactate/normal saline 20mls/kg                      |
| Severe Dehydration   | Two or more of; altered consciousness AVPU<A or lethargy, unable to drink, sunken eyes, return of skin pinch ≥2seconds          | **PLAN C:** **STEP 1:** 30mls/kg Ringer’s lactate over 30minutes if age ≥ 12 months OR over 1 hr if aged < 12 months. **STEP 2:** 70mls/kg Ringer’s lactate over 2.5 hours if age ≥ 12 months OR over 5 hours if age < 12 months |
| Some Dehydration     | Two or more of; drinks eagerly, sunken eyes, restlessness or irritable, return of skin pinch 1-2 seconds                         | **PLAN B:** 75mls/kg ORS over 4hrs                                      |
| No dehydration       | Less than 2 signs. Not enough to classify as some or severe dehydration                                                        | **PLAN A:** 10mls/kg ORS after every loose stool.                         |

Adapted from WHO Pocket book of hospital care for children: Guidelines for the management of common illnesses with limited resources (2nd Edition, 2013) and Kenya Basic Paediatric protocols (January 2016 Edition)

AVPU*- A-alert, V-verbal/voice, P-pain, U-unresponsive. AVPU is a scale used to measure and record a patient’s level of consciousness.
Study population

We analysed data for children aged 1-59 months collected between October 2013 and December 2018. We excluded 10 months of data from a period characterised by health workers strike between December 2016 to November 2017 because there was marked reduction in number of admissions.\textsuperscript{19} We also excluded neonates and those with severe acute malnutrition (SAM) defined as; mid-upper arm circumference (MUAC) <11.5cm for age $\geq$6 months, weight-for-height z-score (WHZ) of $<-3$ standard deviations for children aged $<6$ months, or a clinical diagnosis of SAM. Those with SAM were excluded because they have different management guidelines and dehydration is difficult to diagnose clinically\textsuperscript{20} while for neonates, only minimal data(restricted to information on basic demographic characteristics, diagnoses and admission outcome that is required for routine national health information reporting) are collected and therefore detailed processes of care and admission characteristics could not be described. We also excluded data of non-medical cases including burns, and surgical cases that require specialised care.

The database was reviewed and those with a diagnosis of dehydration at admission or discharge but without diarrhoea as a diagnosis or presenting symptom at admission or discharge were identified. To confirm the absence of diarrhoea and rule out data entry errors, we retrieved a random sample list of patients identified from two hospitals located near Nairobi, where the researchers are based, and one investigator with a medical background visited the hospitals and reviewed the medical records. The records were checked for the presenting symptoms, assessment during admission, in-patient medical notes from the ward rounds, admission and discharge diagnoses, and the data were entered into a separate database. Data collected from medical records were linked using unique patient identifiers to the wider CIN database. We compared findings recorded from medical records review to those in the CIN database specifically for diagnosis or history of diarrhoea.

Data analysis

We described the characteristics of the study population using proportions for binary, categorical and nominal data, means (standard deviations) for normally distributed continuous data and medians (and interquartile ranges) for skewed or ordinal data. The proportion of children with dehydration diagnosis at admission or discharge but without diarrhoea was calculated overall and
for each hospital. We also described fluid management practices (fluid type, volumes, and duration), patient’s characteristics, and underlying diagnoses and case fatality.

**Ethical Considerations**

The CIN project and audit for routine care has been approved by the Kenya Medical Research Institute (KEMRI) Scientific and Ethics Review Unit (SERU) number- (3459), who have approved use of de-identified data for analysis and publication. Primary data belongs to respective hospitals. This work was supported by funds from Wellcome Trust but the funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Patient and Public Involvement**

This study was done without patient involvement. However, the Ministry of Health, county health executives, and all hospital management teams gave permission for this work to be developed and has supported the implementation of the CIN. The study findings have been disseminated to the hospital clinical teams in all the paediatric wards who provide care to the children for whom CIN project is designed.
RESULTS

Demographic characteristics of the study population

A total of 68,204 eligible children were admitted across the 13 study hospitals between October 2013 and December 2018. Figure 1 illustrates selection of the study population. The prevalence of dehydration in children without diarrhoea was 3.0% (2,019/68,204) (range 2.1%-4.3% across hospitals) and this comprised 15.9% (2,019/12,702) of all dehydration cases. Children admitted in hospitals located in areas with high malaria transmission accounted for 45.2% (912/2,019) of the study population. The median age was 14 months (interquartile range, 7-26 months). Sex was documented in 99.0% (2,001/2,019) of the population, 53.3% (1,067/2,001) of whom were male. More than half, 62.1% (1,254/2,019) were febrile (either had a history of fever or temperature >=39°C at admission), while 16.3% (329/2,019) had signs suggestive of impaired circulation shown by either weak pulse, capillary refill of >=3 seconds, temperature gradient or tachycardia (pulse rate >180 beats per minute for children less than 12 months, >160 beats per minute for those aged 12 months and above but below 60 months).  

A total of 106 linked medical records were retrieved for validation from the two hospitals to ascertain the absence of diarrhoea diagnosis in recorded diagnosis or case notes. Review of the case notes showed that none had a diagnosis of diarrhoea or diarrhoea as symptom that may have been missed by the data clerk. Dehydration diagnosis without diarrhoea as recorded in the database and analysed here was therefore accurate.

Based on documented clinical diagnosis, some dehydration was the most common presentation (1,227/2,019, 60.8%), followed by severe dehydration (491/2,019, 24.3%), and shock was least common (142/2,019, 7.0%). Dehydration was not classified in 7.9% (159/2,019) of the cases. Characteristics of study participants are summarised in Table 2. The major clinical diagnoses in this population were pneumonia (50.6%, 1,021/2,019), malaria (35.4%, 715/2,019), anaemia (13.4%, 271/2,019), clinically diagnosed meningitis (11.9%, 241/2,019) and moderate malnutrition (10.5%, 212/2,019). Most patients 93.6% (1,881/2019) had comorbidities in addition to dehydration whereby a co-existence of malaria and pneumonia was the most common 248/2,019 (12.3%), followed by anaemia and malaria 182/2,019 (9.0%) as shown in Figure 2.
The overall case fatality was 12.9% (260/2019) and was directly related to the severity of dehydration-shock (50.0%, 71/142), severe dehydration (20.8%, 102/491), some dehydration (5.5%, 67/1,227). Case fatality for unclassified dehydration was 12.6% (20/159).

Case fatality was 134(11.9%) in children where prescribed any fluid compared to 126 (14.1%) in those without any fluid prescribed. The case fatalities were 125 (16.3%) and 135 (10.8%) respectively in patients prescribed intravenous fluids versus those without intravenous fluids prescriptions. Case fatality was lowest in children prescribed only oral fluids, 9 (2.5%) and moderate for those with oral plus intravenous fluid prescriptions, 15 (7.4%).
Table 2. Characteristics of study participants

| Population characteristics |  |
|----------------------------|---|
| Age in months, median (interquartile range) | 14(7-26) |
| Sex (male %) | 1067/2001(53.3%) |
| Weight (Kg), mean±standard deviation | 9.0±3.7 |
| MUAC (cm), median(interquartile range) | 13.7(12.5-15.0) |

| Clinical characteristics | n/N* (%) |
|--------------------------|---------|
| Capillary refill >2seconds | 128/1287(10.0) |
| Sunken eyes | 546/1464(37.3) |
| Delayed skin pinch | 627/1489(42.1) |
| Weak pulse | 193/1471(13.1) |
| History of Fever | 1239/1614(76.7) |
| Temperature >= 39°C | 240/1439(16.7) |
| Temperature Gradient | 132/1257(10.5) |
| Impaired consciousness | 193/1594(12.1) |
| Cannot drink/breastfeed | 431/1514(28.5) |
| History of vomiting | 1058/1599(66.2) |
| Impaired perfusion | 329/1,578(20.9) |
| Vomits everything | 661/1002(66.0) |
| Age <1 year | 819/2019(40.6) |
| Non-diarrhoeal dehydration/total dehydration | 2019/12702(15.9) |

| Clinical Diagnosis | N=2019,n (%) |
|-------------------|-------------|
| Pneumonia | 1021 (50.6) |
| Malaria | 715 (35.4) |
| Anaemia | 271 (13.4) |
| Meningitis | 241 (11.9) |
| Malnutrition | 212 (10.5) |

| Case fatality | n/N (%) |
|---------------|---------|
| Shock | 71/142(50.0) |
| Severe dehydration | 102/491(20.8) |
| Some dehydration | 67/1227(5.5) |
| Unclassified dehydration | 20/159 (12.6) |

* denotes the study population was 2019, however the denominator for the patients’ characteristics varied based on documentation
**Fluid management practices**

A total 55.8% (1,127/2,019) of children with dehydration had a fluid prescription either intravenous or oral—as summarised in Table 3. For those prescribed intravenous fluids, fluid bolus was prescribed in 3.8% (77/2,019), while maintenance fluid was prescribed in 14.7% (296/2,019) cases. Oral rehydration therapy (plans A or B) without intravenous fluids was prescribed in 17.8% (359/2,019) of cases. However, there were wide variations across hospitals in the use of intravenous fluids ranging from 22.1% to 55.4% or exclusive use of oral fluids, ranging from 7.2% to 38.7%. Nevertheless, use of intravenous fluid in general and fluid bolus were more common in children with severe forms of dehydration. However, notable cases with clinical signs of some dehydration received intravenous fluids, 33.1% (406/1,227), and a few received fluid boluses, 1.2% (15/1,227).

In the febrile group, n=1,254, 65.3% (819/1,254) had a fluid prescribed. Intravenous fluids prescribed in 44.4% (557/1,254) while oral fluid prescribed in 32.6% (409/1,254). Maintenance fluid was prescribed in 18.7% (234/1,254). Use of fluid bolus in this group was 3.6% (45/1,254). Ringer’s lactate and normal saline were the most commonly used intravenous fluids for treatment of shock, (58/74, 78.4%) and (9/74, 12.2%). In participants with shock who had duration of fluid bolus documented, 86.2% (25/29) received bolus fluid rapidly and the rest, 13.8% (4/29), received bolus over 1-2 hours. Median volume of fluid bolus was 20ml per kilogram body weight (interquartile range, 20-30ml). For treatment of severe dehydration, plan C was prescribed in 40.3% (198/491), both step one and two prescribed in 23.6% (116/491) cases. For those younger than 12 months, the median duration of fluid treatment was 6 hours (interquartile range 5-6 hours), while in children 1 year and above the median duration of fluid treatment was 3 hours (interquartile range 3-4 hours). The median volume given was 100ml/kilogram body weight (interquartile range 93-100 ml/kg). Plan B was used in 26.8% (329/1,227) participants with some dehydration, median volume given was 75ml/kilogram body weight (interquartile range 74-75 ml/kg) and was given over a median duration of 4 hours (interquartile range 4-4 hours).
Table 3. Fluid management

| Fluid Therapy   | All Cases (N=2019), n (%) | Shock N=142, n (%) | Severe N=491, n (%) | Some N=1227, n (%) | Not classified N=159, n (%) |
|----------------|---------------------------|-------------------|---------------------|---------------------|----------------------------|
| Any fluid      | 1127 (55.8)               | 89 (62.7)         | 249 (50.7)          | 722 (58.8)          | 67 (42.1)                  |
| IV fluid       | 768 (38.0)                | 83 (58.5)         | 233 (47.5)          | 406 (33.1)          | 46 (28.9)                  |
| Plan C         | 513 (25.4)                | 54 (38.0)         | 198 (40.3)          | 242 (19.7)          | 19 (12.0)                  |
| Fluid bolus    | 77 (3.8)                  | 44 (31.0)         | 18 (3.7)            | 15 (1.2)            | 0.0                        |
| Maintenance fluid | 296 (14.7)            | 24 (16.9)         | 58 (11.8)           | 184 (15.0)          | 30 (18.9)                  |
| Oral fluid     | 562 (27.8)                | 13 (9.2)          | 83 (16.9)           | 439 (35.8)          | 27 (17.0)                  |
| Plan A         | 206 (10.2)                | 10 (7.0)          | 39 (7.9)            | 138 (11.3)          | 19 (12.0)                  |
| Plan B         | 394 (19.5)                | 4 (2.8)           | 45 (9.2)            | 329 (26.8)          | 16 (10.1)                  |
| Both oral and IV | 203 (10.1)              | 7 (4.9)           | 67 (13.7)           | 123 (10.0)          | 6 (3.8)                    |
| Oral fluid only | 359 (17.8)              | 6 (4.2)           | 16 (3.3)            | 316 (25.8)          | 21 (13.2)                  |
| Maintenance fluid only | 12 (0.6)              | 0.0               | 1 (0.2)             | 9 (0.7)             | 2 (1.3)                    |
DISCUSSION

The study was conducted to estimate the prevalence of dehydration from non-diarrhoeal illnesses and establish fluid management practices used routinely by clinicians in the absence of clear guidance. This is the first study locally focusing broadly on dehydration from non-diarrhoeal causes since previous studies have concentrated on shock and impaired circulation which are often adverse effects of untreated dehydration or a consequence of severe sepsis. 7 8 12 14 22 Our study is important especially after concerns generated following findings of the FEAST trial 9 where fluid boluses, which are recommended for treatment of hypovolaemic shock secondary to diarrhoea, 2 4 were shown to be harmful when used to treat shock in those with non-diarrhoeal illnesses. We therefore not only highlight the magnitude of a group of children who may need a different approach to fluid management but also those at risk of potentially harmful therapy.

Our study shows an overall low prevalence of dehydration in patients with non-diarrhoeal illnesses, but it still accounts for about 16% of all cases of dehydration, which is significant in a global context and important when considering children that may be exposed to potentially harmful treatment when liberal fluid therapy is used. Ascertainment through record linkage in two hospitals showed that these were not cases where diarrhoea was present as a symptom or diagnosis but missed at data entry. Fluid treatment, either oral or intravenous, is less frequently used to manage dehydration in the absence of diarrhoea, 55.8% (1,127/2,019) versus 78.2% (6,696/8,562) in children with diarrhoea and dehydration (data not shown, previously described). 23 However, where fluid treatments are given, the route of administration, fluid type, duration of administration and volumes were similar to those recommended in diarrhoea and dehydration. We found some discrepancy in the fluid regimen recorded in patients with various severities of dehydration. For example, there was use of fluid bolus in a child without shock, but we believe that this may be due to rapid change of clinical signs of dehydration. Such children without a diagnosis of shock who received fluid bolus could be those who initially presented with clinical signs of shock at the outpatient department, but the signs rapidly changed after fluid bolus is administered before assessment at the ward, where the characteristics captured in the database are recorded. Case fatality from dehydration in children with non-diarrhoeal illnesses (12.9%, 260/2,019) was also higher than that seen in patients with dehydration and diarrhoea previously. 23 24 Pneumonia and
malaria were common underlying illnesses, and this has also been reported in previous studies.\textsuperscript{8,12}13 25 26

Dehydration in patients without diarrhoea is not surprising because it may be caused by a number of mechanisms such as loss of fluids through vomiting, increased insensible losses from fever and due to high surface area to volume ratio in the under-fives who were the participants in this study.\textsuperscript{1}These mechanisms have been reported in malaria\textsuperscript{12-14} and pneumonia,\textsuperscript{8} which are the two major underlying diagnoses in this study. While less children received rehydration therapy compared to cases with diarrhoea and dehydration, use of similar fluid management approach to that of diarrhoea cases raises concerns of potential harm in malaria,\textsuperscript{9} pneumonia,\textsuperscript{7} and meningitis\textsuperscript{7,27} especially when vascular changes leading to fluid redistribution in vasculature may also be at play. Although this study investigated dehydration rather than impaired circulation as was done in the FEAST study, we think the findings of the FEAST study may have some relevance to this population due to potential in change in condition in real world. Fluid bolus use resulted in increased mortality within the first 48 hours in children admitted with severe infection (57\% of whom had malaria) and impaired perfusion in the FEAST study.\textsuperscript{9} Two well powered systematic reviews where the FEAST study was included, agreed with findings from the FEAST study.\textsuperscript{28,29} Less frequent rehydration therapy in non-diarrhoea illnesses recorded in this study could be a result of cautious use of fluid therapy in non-diarrhoea illnesses such as pneumonia. The high case fatality could be due to underlying diagnoses and dehydration in these cases may be a marker of severity leading to increased risk of death. It is also possible that treatment is wrongly withheld, or a wrong fluid treatment given being responsible for the higher case fatality, but this is only speculative. Fewer children with dehydration without diarrhoea received fluid therapy and it’s not clear if this decision is correct and fluid regimen to use in non-diarrhoeal cases is contentious. Nevertheless, these findings warrant further attention given the findings in the FEAST study and its significance to the study population. We have previously shown low use of fluid boluses in these hospitals,\textsuperscript{30} which is reassuring, but data analysed captured a period before widespread dissemination of the new WHO fluid guidelines\textsuperscript{4} and results in this study are reassuring.

Hospitals in this study receive regular feedback on care processes given to admitted children and the network also has data quality assurance procedures in place. We are therefore confident that the data is of good quality and this was reinforced by the validation from the file linkage in this
study. CIN procedures have also improved documentation of assessment, diagnosis, classification, and treatments and this allows for the analysis presented here which may be difficult to repeat in settings without activities such as done within CIN.\textsuperscript{31} However, the findings are still generalisable because of diversity of hospitals involved and use of routine data rather than those collected under research conditions.

These results highlight varied practice in the absence of clear guidance for use by frontline clinicians in resource poor settings, who are often junior clinicians. We recognise that guidelines cannot cover all imaginable clinical scenarios, but fluid treatment is quite a common practice in hospitals and guidance for this group may be necessary. However, this will only be possible after definitive studies to address their fluid therapy given the concerns seen in the FEAST study.\textsuperscript{32} While these children did not have diarrhoea, even those with dehydration secondary to diarrhoea frequently present with other conditions where cautious fluid management is advised.\textsuperscript{23} Therefore, further studies may also be necessary to investigate appropriate fluid management for those with diarrhoea and dehydration complicated with other illnesses.

Limitations

Our study was limited in several ways; some treatment might have been documented but not given or administered but not documented and we can’t ascertain actual administration. Use of registry data is also known for its limitations with ascertainment and selection biases being persisting concerns. We also used clinician diagnoses without checking whether these reflected correct diagnoses based on clinical signs and there can be misdiagnosis due to errors, clinical inexperience, and lack of adequate knowledge.\textsuperscript{33}

CONCLUSION

Sixteen percent of children hospitalised with dehydration do not have diarrhoea. Although dehydration is uncommon in children without diarrhoea, the case fatality is higher compared to that in children with diarrhoea. Clinicians are less likely to use fluids for treatment of dehydration when there is no diarrhoea, but they use same fluid regime like that for diarrhoeal cases when they prescribe fluid therapy, which is potentially harmful. Efforts to promote compliance with guidance
in routine clinical settings should recognise special circumstances where guidelines do not apply and in need for further evidence.

AUTHORS CONTRIBUTIONS

SA and ME conceptualised and designed the study with contribution from JA, DG and AA. SO collected case notes review data. SO analysed the data and drafted the initial manuscript with input from SA and other co-authors. All authors reviewed and provided input into the final version of the manuscript.

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COMPETING INTERESTS

None

DATA SHARING STATEMENT

The source data are owned by the Kenyan Ministry of Health and County Governments. Users who wish to reuse the source data should make a request through the KEMRI-Wellcome Trust Research Programme data governance committee.

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**LEGENDS TO TABLES AND FIGURES**

Figure 1: Flow diagram showing patient selection.

Figure 2: Venn diagram showing sets of combinations of top 4 comorbidities in addition to dehydration. Other diagnoses not in top 4 are denoted by “Others”.

Table 1: Guidelines for management of dehydration for children aged ≥ 1 month (excluding severe malnutrition).

Table 2: Characteristics of study participants

Table 3: Fluid management
Figure 1: Flow diagram showing patients selection

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Figure 2: Venn diagram showing sets of combinations of top 4 comorbidities in addition to dehydration. Other diagnoses not in top 4 are denoted by "Others"

228x127mm (300 x 300 DPI)
The STROBE statement, that should be reported in observational studies.

| Item No. | STROBE items                                                                 | Location in manuscript where items are reported |
|----------|-----------------------------------------------------------------------------|-------------------------------------------------|
| 1        | (a) Indicate the study’s design with a commonly used term in the title or the abstract | Page 1, Title and page 2, paragraph 2.           |
|          | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | Page 2, paragraph 1 to 5                         |
| 2        | Explain the scientific background and rationale for the investigation being reported | Page 4, paragraph 1                              |
| 3        | State specific objectives, including any prespecified hypotheses            | Page 4, paragraph 2                              |
| 4        | Present key elements of study design early in the paper                     | Page 4, paragraph 3; to page 5 Methods: Study design and setting sub-section |
| 5        | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Page 4, paragraph 3; to page 5 Methods: Study design and setting sub-section |
| 6        | (a) Give the eligibility criteria, and the sources and methods of selection of participants | Page 6, paragraph 1 and 2 Methods: Study population subsection |
| 7        | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. | Not applicable                                   |
| 8        | For each variable of interest, give sources of data and details of methods of assessment (measurement). | Page 5, paragraph 1 Methods: Study design and setting |
|          | Describe comparability of assessment methods if there is more than one group | Not applicable                                   |
| 9        | Describe any efforts to address potential sources of bias                   | Page 5, paragraph 1 Methods: Study design and setting Addresses efforts to minimise information bias. |
| Study size | 10 | Explain how the study size was arrived at | Page 6, paragraph 1 & 2
Methods: Study population
We used all records meeting inclusion criteria during the study period, hence no sampling required |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why | Page 6, paragraph 3 and page 7 paragraph 1
Methods: Data analysis |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding | Page 6, paragraph 3 and page 7 paragraph 1
Methods: Data analysis |
| | | (b) Describe any methods used to examine subgroups and interactions | Not applicable |
| | | (c) Explain how missing data were addressed | Not applicable |
| | | (d) If applicable, describe analytical methods taking account of sampling strategy | Not applicable |
| | | (e) Describe any sensitivity analyses | Not applicable |
| Results | | | |
| Participants | 13 | (a) Report the numbers of individuals at each stage of the study (e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed)
(b) Give reasons for non-participation at each stage.
(c) Consider use of a flow diagram | File upload 3: Study population flow chart. |
| Descriptive data | 14 | (a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders
(b) Indicate the number of participants with missing data for each variable of interest | Page 8 to page 10
Results: Demographic characteristics of the study population and Table 2 |
| Outcome data | 15 | Report numbers of outcome events or summary measures | Page 11 to page 12 |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which | Not applicable |
confounders were adjusted for and why they were included

(b) Report category boundaries when continuous variables were categorized

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses 17 Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses

Not applicable

Discussion

Key results 18 Summarise key results with reference to study objectives

Page 13, paragraph 2 Discussion

Limitations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias

Page 15, paragraph 3 Discussion: Limitations

Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence

Page 14 Discussion

Generalisability 21 Discuss the generalisability (external validity) of the study results

Page 14, paragraph 2 and Page 15, Discussion paragraph 5

Other Information

Funding 22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

Page 17, paragraph 1 Funding section