RESEARCH ARTICLE

The prevalence, incidence and mortality associated with intra-abdominal hypertension among patients in intensive care units of a low-income country: a cohort study [version 1; peer review: 4 approved with reservations]

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Abstract

Background: Intra-abdominal hypertension (IAH) is sustained increase in intra-abdominal pressure (IAP) ≥ 12 mmHg in adults and ≥ 10 mmHg in children. IAH has been noted to be associated with increased morbidity and mortality among critically ill patients. Measurement of IAP is common among at risk patients in the developed world. However, it has not received due attention in the majority of intensive care units (ICUs) in low-income countries, Uganda being one of these. This is evidenced by paucity of data and lack of protocols from the Ugandan Ministry of Health. This multi-center study was thus conducted to assess the prevalence, incidence and mortality associated with IAH among patients admitted to Ugandan ICUs.

Methods: A multi-center prospective cohort study was conducted from September 2017 to February 2018 at three ICUs in Uganda. We consecutively enrolled 126 patients into the study. IAP was measured using the Harrahil manometer technique. Categorical variables were analyzed using the Chi square test and continuous variables analyzed using the t-test and Man Whitney test. The prevalence and incidence were determined using proportions and mortality was determined using survival analysis.

Results: The median age was 33 years (26-48.5) for the patients without IAH and 42 years (29-55) for those with IAH. The majority of the patients were male and 9.6% of the patients were below 18 years. The prevalence of IAH was 62.7 (CI 54.1-71.3), whereas the 24 hour and 72 hour incidence of IAH was 9.3% (CI 1.3-17.2) and 14.3 % (CI 4.1-24.4), respectively. Mortality was higher in patients with IAH compared to those without (p-value 0.003 and 0.028, mean and

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maximum IAP, respectively).

Conclusion: We found a high prevalence and incidence of IAH among critically ill patients, associated with a high mortality. Routine screening for IAH can preempt management strategies to mitigate this.

Keywords

Prevalence, IAH, IAP, ICU, Mortality

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Introduction

Intra-abdominal pressure (IAP) is defined as the steady state pressure within the abdominal cavity bounded by the abdominal muscles and diaphragm¹. It is affected by body weight, posture, tension of abdominal muscles and movement of the diaphragm². Normal IAP among critically ill patients ranges from 5–7mmHg³.

In 2006, the World Society on Abdominal Compartment Syndrome (WSACS) established consensus definitions for intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS). Thus IAH is the steady state pressure concealed within the abdominal cavity, while ACS is a sustained IAP of >20mmHg with or without an abdominal perfusion pressure of <60mmHg that is associated with a new organ dysfunction⁴.

Levels of IAH that have been clearly documented in laboratory settings to dramatically influence organ dysfunction stay unrecognized, unappreciated and untreated every day in intensive care units (ICUs) across the world⁵.

In Africa, IAH has not been widely studied. Case reports concerning the diagnosis and management of patients with IAH have been published in South Africa, indicating the benefits of early recognition and intervention among these patients⁶.

Raised IAP is caused by trauma, intra-abdominal or retroperitoneal hemorrhage, peritonitis, repair of incision hernias and massive fluid resuscitation, which are common conditions in ICUs⁷.

Elevated IAP among the critically ill is associated with significant morbidity and mortality. Given the broad range of etiological factors for IAH, a high index of suspicion and low threshold for IAP measurement appears appropriate for a patient possessing any of the risk factors. IAP measurement is both diagnostic in detecting IAH as well as therapeutic, as IAP guided resuscitation has been shown to correlate with improved survival⁸.

In Uganda, IAH prevalence has been studied among burns and post-surgical patients associated with high mortality. However, there is paucity of data concerning the prevalence of IAH amongst patients admitted to Ugandan ICUs despite the fact that most of these critically ill patients have risk factors for IAH. IAP measurement is not done routinely in ICUs in Uganda and thus interventions for patients with IAH cannot be easily determined. Prediction of development of IAH amongst critically ill patients based on clinical presentation remains a challenge and its management depends on serial IAP measurement amongst patients at risk. Unmanaged IAH results in respiratory, cardiac and renal complications that result in an increased length of stay in the ICU, increased ventilator requirements and thus, high hospital expenditure on ICU patients.

Methods

Ethical statement

This study was approved by the Institutional Review Board of the School of Medicine Research and Ethics Committee of

Makerere University (reference number REC REF 2017-091). A written consent to carry out the study was obtained from conscious patients or their next of kin. A waiver of consent was obtained for critically ill patients without proxies. Physicians responsible for the care of patients in the ICUs were informed once IAH was diagnosed in a study participant and management of IAH was left to the discretion of the physician.

Study background

We conducted a prospective multicenter cohort study among critically ill patients between September 2017 to February 2018 at Mulago National Referral ICU, International Hospital Kampala ICU and Nakasero Hospital Limited ICU in Kampala city, Uganda.

Sample size and eligibility criteria

We consecutively included all patients admitted to the three intensive care units during the study period who were above one year of age and were admitted for more than 24 hours. Among the patients excluded from the study were infants and neonates due to varying catheterization techniques, which were incompatible with the manometer used in IAP measurement. Patients with contraindications to intra-vesicle pressure measurement including those with pelvic fractures, hematuria, or neurogenic bladder were also excluded. Pregnant women were excluded due to variance in IAP at different gestation ages and paucity of data concerning grading of IAH in this patient population at the time of the study.

Patient assessment

The recruited patients were reviewed at T0, T24, and T72 hours. T0 was defined as 0-3 hours post ICU admission, T24 was defined as 24 hours post ICU admission, and T72 as 72 hours post ICU admission. We used a pretested questionnaire⁹ to collect data on the day of admission, at T24 and T72 hours and on the day of death/ discharge from the ICU. The questionnaire was pre-tested by the principal investigator (PI) and trained research assistants who were critical care nurses a month prior to commencement of data collection on 12 patients, four from each ICU to assess ease of administration of the questionnaire while conducting the study. No modifications of the questionnaire were required. The questionnaire was administered by the PI and trained research assistants. The data was obtained from the patients' records and directly measured values. The data collected from patients' records included: patients' age and gender, referral source, indication for ICU admission, HIV sero-status, mode of ventilation, ventilation period, length of ICU stay, date of death/discharge from the ICU, 24-hour and cumulative fluid balance. The PI and research assistants measured and recorded the set of vitals at admission, GCS score, and IAP measurements. The mean and maximum IAP were calculated and recorded by the PI and research assistants.

The patients were catheterized using a two-way Foleys catheter, the urinary bladder drained and 20ml (1ml/kg for the pediatric patients) of normal saline instilled in the bladder through a manometer connected directly to the urinary catheter. The manometer was held 30 cm above the symphysis pubis (iliac crest, mid-axillary line for pediatric patients) and the pressure

read off from the saline water column. The pressure was measured in millimeters of mercury at the end of expiration. This was done at T0, T24 and T72 hours. To eliminate errors, three readings were taken at each time and the average recorded.

There was no further patient contact until day of discharge from ICU or 28th day in the ICU, when patients' status of survival or death was recorded.

For patients who were discharged/dead at 72 hours or 28 days, the initial (last) observations were considered.

Data management and statistical analysis

The sample size of 111 was calculated using the Keish and Leslie formula. A 10% increment was made to cater for loss to follow up bringing the estimated sample size to 122. We were able to analyze data for 126 patients at the end of the study period.

Data was captured into a database generated using EPI DATA version 3.1. Data was analyzed using STATA version 14.1 and was adjusted for clustering at the level of the hospital. Continuous variables were summarized using means, standard deviations, if parametric, and medians, with interquartile ranges if non-parametric. Categorical variables were summarized using frequencies, proportions, and percentages.

The event for Kaplan Meier curve was mortality and the time to event was measured as days to mortality. The graph was compared for patients who had IAH and those who did not have IAH.

Results

Of the 200 patients that were admitted to the three ICUs during the study period, 126 patients met the eligibility criteria (Figure 1). Of the study participants, 90% were adults, of which 59.5% were male⁹. The median age was 33 years (26-48.5) for

Figure 1. Recruitment scheme.

the patients without IAH at baseline and 42 years (29-55) for those with IAH. The majority of the patients were admitted from the emergency room and respiratory failure was the predominant reason for ICU admission. Most of the patients admitted

to the ICU had both positive 24 hour and cumulative fluid balance. All patients who had acute renal failure at admission had IAH and so did the majority of patients with a head injury, those that had been sedated and those with sepsis (Table 1 and Table 2).

Table 1. Showing baseline clinical characteristics among patients admitted to three Ugandan ICUs.

Variable name	No IAH (N= 56)	IAH (N=70)	p-value
	N (%) / Median (IQR)		
Sex			
Male	36(48.0)	39(52.0)	
Female	20(39.2)	31(60.8)	0.330
Age	33.5(26.0-48.5)	42.0(29.0-55.0)	0.048
Location before transfer to ICU			
Emergency/casualty	22(47.8)	24(52.2)	
Operating theatre	22(56.4)	17(43.6)	
Obstetrics/gynaecology theatre	0(0.0)	1(100.0)	
Medical ward	3(25.0)	9(75.0)	
Surgical ward	1(25.0)	3(75.0)	
Obstetrics/gynaecology ward	1(100.0)	0(0.0)	
Another hospital	7(31.8)	15(68.2)	0.180
Surgical type			
Abdominal	7(43.8)	9(56.3)	
Thoracic	3(42.9)	4(57.1)	
Neuro	16(69.6)	7(30.4)	
Orthopedics	2(50.0)	2(50.0)	
Endocrine	2(100.0)	0(0.0)	
Obstetrics/gynaecology	2(33.3)	4(66.7)	
Urology	0(0.0)	1(100.0)	
Other type	1(33.3)	2(66.7)	
No surgery	23(35.9)	41(64.1)	0.134
Oxygen saturation	98.0(96.0-99.5)	98.0(94.0-99.0)	0.499
Received oxygen			
Yes	52(44.4)	65(55.6)	
No	4(44.4)	5(55.6)	0.631
Patient on mechanical ventilation			
Yes	38(41.8)	53(58.2)	
No	18(52.9)	16(47.1)	0.263
Duration of mechanical ventilation (days)	4(3-10)	4(2-10)	0.510

ICU, intensive care unit; IAH, intra-abdominal hypertension; IQR, interquartile range.

Table 2. Showing baseline clinical characteristics of the study participants.

Variable name	No IAH (N= 56)	IAH (N=70)	p-value
	N (%) / Median (IQR)		
Reasons for ICU admission			
Stroke	5(8.9)	9(11.1)	0.486
Respiratory distress/ failure	33(38.82)	52(61.2)	0.068
Hypotension/ shock	4(36.4)	7(63.6)	0.753
Renal failure	0(0.0)	11(100.0)	0.001
Severe trauma	4(66.7)	2(33.3)	0.405
Seizures	7(44.4)	70(55.6)	0.108
Pre-eclampsia/ eclampsia	1(50.0)	1(50.0)	1.000
Post-operative high care	20(57.1)	15(42.9)	0.075
Head injury	19(65.5)	10(34.5)	0.009
Sepsis	2(44.4)	23(92.0)	<0.001
Post cardiac arrest	5(62.5)	3(37.5)	0.465
Altered mentation	17(63.0)	10(37.0)	0.029
Other reasons*	10(33.3)	20(66.7)	0.161
Working diagnosis in ICU			
Head injury	14(50.0)	14(50.0)	0.502
Sepsis	1(3.9)	25(96.2)	<0.001
ARDS	3(23.1)	10(76.9)	0.142

The prevalence of IAH for all the patients recruited in the study was high 62.7% (CI 54.1-71.3). Of the 48 patients who died, 36 had IAH (Table 3).

The 72-hour incidence of IAH was higher than that at 24 hours. The patients below 18 years had a higher incidence at 72 hours compared to adults (Table 4).

Following multi-variate analysis, sepsis was found to be a statistically significant risk factor associated with IAH (Table 5).

Of the 48 patients who died, 36 had IAH. When either mean IAP or maximum IAP that meets the definition of IAH was considered, the risk of dying among patients admitted in ICU was significantly higher in those with IAH compared to those with no IAH, p-value 0.003 and 0.028 for mean and maximum IAP, respectively (Table 6).

The median survival time of patients with IAH was 11 days, while patients without IAH survived for more than 14 days.

Variable name	No IAH (N= 56)	IAH (N=70)	p-value
	N (%) / Median (IQR)		
Cardiac failure	0(0.0)	4(100.0)	0.128
Renal failure	0(0.0)	10(100.0)	0.002
Pneumonia	5(35.7)	9(64.3)	0.486
Other types**	29(44.6)	36(55.4)	0.968
Hospital			
1	40(61.5)	25(38.5)	
2	6(19.4)	25(80.7)	
3	10(33.3)	20(66.7)	<0.001
GCS			
≤ 8	25(47.2)	28(52.8)	
> 8	29(49.2)	30(50.9)	
Sedated	2(14.3)	12(85.7)	0.048
HIV status			
Negative	26(47.3)	29(52.7)	
Positive	2(33.3)	4(66.7)	0.678

IAH, intra-abdominal hypertension; IQR, interquartile range; ICU, intensive care unit; ARDS, acute respiratory distress syndrome; IHK, International Hospital Kampala; GCS, Glasgow Coma Scale; HIV, human immunodeficiency virus.

* Other reasons: electrolyte imbalances, organophosphate poisoning.

** Other types: intra-cranial hemorrhage, sickle cell crisis, anterior fossa duraplasty, type I respiratory failure, tuberculosis pericarditis, cerebellar lesions of unknown origin, organophosphate poisoning, laryngeal lesion, cancer of the cervix, post cardiac arrest, HELLP syndrome, seizure disorder, polytrauma.

More patients who had IAH died than those without, especially in the first 10 days of ICU stay. After day 20, patients without IAH were more likely to survive, whereas those with IAH were even more likely to die (Figure 2).

Discussion

We set out to determine the prevalence, incidence and mortality associated with intra-abdominal hypertension among patients admitted to three ICUs in Kampala Uganda. Our secondary objective was to determine the outcomes of patients with IAH, of which duration of mechanical ventilation, length of ICU stay and 28-day ICU mortality were considered. The median age of the study population was 38, which is similar to that reported in a study done in Kenya¹⁰; however, studies that have been done in the developed world have reflected a much older population^{11,12}.

Studies conducted in Uganda concerning IAH have been in burns patients and surgical cases and involved a single center¹³. This is the first multi-center study to be conducted in three ICUs in Uganda.

Table 3. Showing overall prevalence of intra-abdominal hypertension among selected categories of patients admitted to three Ugandan ICUs.

Variable	95% CI	P value
Overall	62.7(54.1-71.3)	
Age		
Below 18	66.7(35.4-98)	0.793
18 and above	62.8(53.8-71.9)	
Hospital		
1	46.2(33.7-58.6)	0.000
2	90.3(79.3-100)	
3	70(52.6-87.4)	
Gender		
Male	58.7(47.3-70.1)	0.256
Female	68.6(55.4-81.8)	
Working diagnosis		
ARDS		
Yes	84.6(61.9-100)	0.084
Sepsis		
Yes	92.3(81.3-100)	0.000
24 hour fluid status		
Positive balance	67.3(57.9-76.8)	0.02
Mechanical ventilation		
Yes	64.8(54.8-74.8)	0.358

ICU, intensive care unit; CI, confidence interval; ARDS, acute respiratory distress syndrome.

Table 4. Showing 24-hour and 72-hour incidence of intra-abdominal hypertension among 126 patients admitted to three Ugandan ICUs.

Variable	Incidence (95% CI)	
	At 24 hours	After 72 hours
Overall	9.3(1.3-17.2)	14.3(4.1-24.4)
By age		
Below 18	0	20(0-75.5)
18 and above	10.2(1.4-18.9)	13.6(3-14.1)

ICU, intensive care unit; CI, confidence interval.

We found a high prevalence of IAH among patients admitted to these ICUs, slightly above that found in a Kenyan mixed ICU, although within the range of what has been studied worldwide^{10,14}. The incidence of IAH was also high, with sepsis found to be a risk factor for IAH in ICUs within our setting.

The duration of mechanical ventilation and length of stay in the ICU was longer in patients with IAH compared to those without; however, this was of no statistical significance. The majority of the patients who died during the study period had IAH and this has been evident in other studies, which have reported high mortality in these patients.

The prevalence of IAH was found to be high among the critically ill patients admitted in the three Ugandan ICUs. This is in line with similar studies that have been carried out elsewhere in East Africa¹⁰ and in high-income countries^{12,15}. At admission all patients admitted with acute renal failure had IAH at baseline measurement. This may signify earlier development of IAH prior to referral to the ICU; however, conclusions cannot be drawn as IAP measurements were not made outside the ICU. In other studies, acute renal failure has been reported as a complication of IAH in various categories of patients¹⁶⁻¹⁸.

The incidence of IAH at 24 hours and 72 hours among admitted patients was 9.3% and 14.3%, respectively, findings of which are similar to that done by Ghulam *et al.* in a mixed ICU where they found the incidence to be 10% among 83 patients recruited in the study¹⁹. Other studies, however, have found higher incidence rates¹⁴. A lower incidence may have been due to protocols practiced in the ICUs that lessen development of IAH. The onset time of IAH is still a challenge and given that these were point measurements, high IAP readings may have been missed between measuring times. Continuous IAP measurement using transducers for the duration of stay of patients at risk of IAH as recommended by WSACS thus remains to be studied. The prevalence was significantly higher than the incidence and pre-ICU patient status; lack of routine screening of at-risk patients may have been a contributing factor.

We found sepsis to be a significant risk factor for IAH among patients enrolled in our study and this is in line with the risk factors that were identified by the WSACS²⁰. Unlike in other studies, positive 24 hour and cumulative fluid balance were not significantly associated with IAH. This may be due to the differences in patient population, and interventions done in particular ICUs, such as targeting a negative fluid balance as part of their protocol. This study did not evaluate preventive and intervention strategies done in these units, which may have affected the association of IAH with factors as defined by WSACS. The small sample size might also have been contributory to this effect.

Table 5. Showing bivariate and multivariate analysis for factors associated with intra-abdominal hypertension among patients admitted to Ugandan ICUs.

Variable	n/N (%)	Crude OR (95%CI)	p-value	Adjusted OR (95% CI)	p-value
Severe head injury					
No	67/97(69.1)	1		1	
Yes	12/29 (41.4)	0.3(0.1-0.7)	0.008	0.9(0.3-2.9)	0.873
Sepsis					
No	49/92(53.3)	1		1	
Yes	30/34(88.2)	9.2(2.1-41.3)	0.004	12.3(2.3-66)	0.004
24-hour fluid balance					
Negative	10/24(41.7)	1		1	
Positive	66/98(67.4)	2.9(1.2-7.2)	0.023	2.5(0.9-7.6)	0.092
Shock					
No	69/115(60)	1		1	
Yes	10/11(90.9)	6.7(0.8-53.9)	0.075	5.3(0.4-79.9)	0.225
ARDS					
No	68/113(60.2)	1		1	
Yes	11/13(84.6)	3.6(0.8-17.2)	0.103	1.4(0.2-10.1)	0.719
Need for vasopressors					
No	63/108(58.3)	1		1	
Yes	16/18(88.9)	5.7(1.2-26.1)	0.025	3.2(0.4-23.9)	0.256

ICU, intensive care unit; OR, odds ratio; CI, confidence interval; ARDS, acute respiratory distress syndrome.

Table 6. Showing the length of ICU stay, duration of mechanical ventilation and 28-day ICU mortality among patients recruited in the study.

Outcome	N (%) / Median (IQR)					
	Mean IAP			Max IAP		
	No IAH	IAH	P-value	No IAH	IAH	P-value
Discharge status						
Alive	40(76.9)	37(50.7)		36(73.5)	41(54.0)	
Died	12(23.1)	36(49.3)	0.003	13(26.5)	35(46.0)	0.028
Length of ICU stay (days)	6(3-18)	4.5(3.0-12.0)	0.3021	5.5(3.0-16.5)	5(3.0-12.0)	0.3928
Duration of mechanical ventilation (days)	6(3-10.5)	4(2.0-9.0)	0.2667	5(3.0-10.0)	4(2.0-10.0)	0.3657

ICU, intensive care unit; IQR, interquartile range; IAP, intra-abdominal pressure; IAH, intra-abdominal hypertension.

In a study carried out in 11 ICUs on 130 patients, the prevalence of IAH was found to be higher among patients that required mechanical ventilation than those who did not²¹. This was in contrast to our findings, where we found no statistical

significance of mechanical ventilation or its duration with IAH. The higher mortality rate in patients with IAH compared to those without may have contributed to less days spent on mechanical ventilation.

Figure 2. Kaplan Meier survival analysis curve.

The mean ICU stay in patients admitted during the study period was nine days and no difference was found between those that had IAH and those that did not. However, in other studies worldwide patients with IAH have been found to stay significantly longer than those without^{2,22,23}. The findings may be explained by the fact that the majority of patients with IAH died faster than those without, hence contributing to the shorter duration of stay in the ICU.

In this study, more patients who had IAH died than those without and IAH had a statistically significant association with risk of dying. This is in agreement with studies carried out in Uganda and worldwide^{12,24}. This study did not follow up patients post ICU discharge and therefore, post ICU mortality in these patients was not detected as it was in other studies and hence mortality may be higher if this is also assessed. The presence of IAH at admission has also been found to be a prognostic indicator for mortality in critically ill patients²⁵. The prevalence of IAH was high at admission among the patients recruited in this study and whether it is a prognostic indicator for mortality in our setting remains to be further studied.

Conclusion

The prevalence and incidence of IAH were found to be high, associated with high mortality among patients admitted to

Ugandan ICUs. The findings of our study are meant to highlight the disease burden in the critically ill, to pave way for further research and development of protocols for screening, preventing and managing IAH in our ICUs.

Data availability

Underlying data

Open Science Framework: The prevalence, Incidence and Mortality Associated with Intra-Abdominal Hypertension Among Patients in Intensive Care Units of a Low Income Country: a cohort study <https://doi.org/10.17605/OSF.IO/XVH6Y9>.

This project contains the following underlying data:

- Copy of IAH_data.xlsx

Extended data

Open Science Framework: The prevalence, Incidence and Mortality Associated with Intra-Abdominal Hypertension Among Patients in Intensive Care Units of a Low Income Country: a cohort study <https://doi.org/10.17605/OSF.IO/XVH6Y9>.

- Copy of the questionnaire.docx

Data are available under the terms of the [Creative Commons Zero "No rights reserved" data waiver](#) (CC0 1.0 Public domain dedication).

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Wangari Waweru-Siika

Department of Anaesthesia, Aga Khan University, Nairobi, Kenya

This was a prospective multicenter cohort study conducted across 3 ICUs in Uganda to assess the prevalence, incidence and mortality associated with IAH in this part of the world. This is an interesting article that assesses an aspect of critical care that is often neglected in LMICs.

Study setting:

- A description of the 3 hospitals showing how similar or different they are would have been interesting to provide e.g. are these all teaching hospitals, intensivist-led, well-resourced, etc.? The highly significant difference in prevalence of IAH between the 3 facilities warrants some discussion to shed light on what is likely to have contributed to these findings.
- Sample size: It is unclear what the basis for the sample size calculation was. This is particularly important given that the authors later state that their study may have been underpowered to make certain conclusions due to the small sample size.

Methodology:

- The objectives of the study (primary and secondary) need to be stated here.
- Please include a statement to show what position patients were in when intra-abdominal measurements were being taken i.e. supine or semi-recumbent? If supine, how were the 28 with head injury catered for? If semi-recumbent, how many degrees head up?
- Why was it necessary to assess HIV status and not any other co-morbidity? Is there any relationship between IAH and HIV?
- Severity of illness scores are not provided. It would have been useful to share these to help the reader understand whether IAH is an independent predictor of mortality.
- The statistical analysis section lacks sufficient detail e.g. regression analysis, level of significance chosen, etc. Tests of significance mentioned in the abstract do not appear in

the body of the manuscript.

- The incidence aspect of this study is unclear. What were the median baseline IAH readings and how did they progress over time in this cohort?

Results:

- Please provide the values of the measurements obtained at T0, T24 and T72 (mean, range, etc).
- Are the prevalence figures in Table 3 percentages?

Study definitions:

- What was the study definition of a positive fluid balance? Why was this only assessed at 24 hours and not at 72 hours? The finding that there was no association between positive fluid balance and IAH may be because this was assessed too early in the course of their ICU stay and also because it is likely that patients with an insignificant positive fluid balance were mixed with those whose fluid balance would be considered clinically significant.#
- How was loss to follow up defined? There was no follow-up after ICU discharge.
- In the GCS category, some 13 patients defined as sedated are included and the presence and absence of IAH assessed. It is not entirely clear what this refers to and why they are treated as a sub-group. Were all the other patients (even those with GCS ≤ 8) not sedated?

Discussion:

- How did these findings compare with the quoted Ugandan studies that looked at burns and surgical patients?

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Quality of critical care and critical care outcomes in low-resource settings.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 20 November 2020

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Jacob Ninan

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Ognjen Gajic

METRIC-Multidisciplinary and Translational Research in Intensive Care Medicine, Mayo Clinic, Rochester, MN, USA

The authors have attempted to identify the prevalence of, and mortality associated with intra-abdominal hypertension in patients from Uganda by performing a multicenter prospective cohort study. The authors should be congratulated for a research effort to 1) foster a culture of research, 2) close large knowledge gaps, and 3) inform the practice in low income African setting. The following weaknesses were identified in the review in addition to those previously pointed by the reviewers.

Abstract:

Please correct the spelling error “Mann” rather than Man_Whitney

“survival analysis” is meaningless in the ICU (dying slower is not better than dying faster); simple hospital or 60 day mortality is more meaningful

The “prevalence” of IAH was 62.7 (CI 54.1-71.3), is NOT clear, is it an overall percentage?

In addition to providing % please provide the numbers (how many patients out of XX had IAH and how many n(%) died. It is unclear what “mean and maximum” with p value actually mean,,,,,

The recommendation for routine screening for IAP with manometry of ALL patients is not supported by this study, would not use in the abstract conclusions

Introduction:

The definition of abdominal compartment syndrome was provided; however, the definition of intra-abdominal hypertension was not. No mention of the intraabdominal pressure cut-off used to screen the patients has been mentioned in the methods section. Did the study evaluate for the presence of abdominal compartment syndrome or intraabdominal hypertension?

Methods:

Inclusion criteria: Prevalence, etiology and mortality rates in pediatric and adult population due to IAH are probably different; hence either pediatric or adult population need to have been studied. The sample size calculation would also be dependent on their respective prevalence.

Procedure of IAP measurement: When a standardized approach to performing intraabdominal pressure measurement is available, this should be used to prevent ambiguity in result interpretation. An explanation would need to be provided as to why the manometer was held 30cm above the symphysis pubis.

The definition of mean intraabdominal pressure and maximum intraabdominal pressure was not provided in the methods section.

Measurement of bladder pressure is known not to be reliable in non-paralyzed patients. It is not clear how many patients were paralyzed for the measurements

Survival analysis (KM curve) is NOT appropriate for ICU patients, simple mortality is preferable
I am not sure that adding incidence to prevalence is useful in this study

Results:

The mean/median intraabdominal pressure among the group of patients with and without intraabdominal hypertension was not mentioned.

The prevalence of IAH in the various hospital ICUs vary between Table 2 and Table 3. Please explain

In table2: The HIV status among patients with and without IAH do not add up to their respective n, please check and clarify

A diagnosis of intraabdominal hypertension does not portend a poor prognosis. It would be informative to the reader if the counts/percentages of patients in the various stages of intraabdominal hypertension were included in the results. The mortality rates in these various stages would be valuable.

Table 3 is not needed; Table 6 can be simply spelled out as text.

Table 5 is the most informative, yet some other determinants of IAH are missing. Is sepsis mostly abdominal sepsis? (you would not expect IAH from pneumonia...). How about GI failure/ileus/NGT use etc.

Discussion:

Despite generating results, an inference for the cause of these results has not been provided. It is somewhat unclear how to interpret your findings? What potentially preventable factors could be responsible? How much IAH actually contribute to bad outcome? Is it an incidental finding in otherwise sick patients OR there is something we can do about it? Interpretation in relation to previously published studies in other parts of the world would be useful.

Minor suggestions:

- "Of the 48 patients who died, 36 had IAH (Table 3)." – There is no mention of mortality in table 3 [Page 6]
- Printer's devil:

○

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Critical care

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Reviewer Report 16 November 2020

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David G. Greenhalgh

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² University of California, Davis, Davis, CA, USA

The authors review the prevalence of IAH in patients in ICUs in Uganda. Overall, the paper is well done and interesting. While the authors may not be able to provide the following information, it would improve the paper:

1. While IAH is important, how many of those patients developed Abdominal Compartment Syndrome (ACS)? In other words, did the IAH progress to IAH? Or did the patients die of other problems not related to IAH? Were there any signs of ACS such as decreased urine

output or increased peak inspiratory pressures? This information is important since physicians would need to know if IAH progresses to the more severe ACS.

2. Another issue that should be addressed is whether there was any correlation between volume of fluid resuscitation in association with IAH. Did patients who received large volumes of fluid have more IAH?

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: I am a burn surgeon who has written several papers on ACS. I do research in resuscitation, response to injury and wound healing

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 29 October 2020

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Theogene Twagirumugabe

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² University Teaching Hospital of Butare, Butare, Rwanda

Thanks for the trust invested in me to review this manuscript. I found the topic of great interest in the ICU domain and the authors are to be congratulated for having tried to unearth some aspects of this syndrome in a low-resource setting. This will probably add a piece of evidence to the existing knowledge on the profile and epidemiology of critical illness in those low-resource settings. I have read with much interest this manuscript and found it to be commendable for indexing, though there are major issues to be addressed prior to the acceptance for indexing:

1) The title:

- The combination of “prevalence, incidence and outcome” in the title is not suitable as these aspects refer to different study designs that are not used in this study. “Prevalence and outcome” may have sufficed if the sample size was big enough, which it is not the case but the study can be seen as an exploratory one subject to be comforted by a larger study.

2) The abstract:

- The format is good but in the “Methods” section, the authors described the statistics used to compare variables with regard to an outcome that is not well specified. Also the statistics were not clearly mentioned in the core text of the manuscript.
- In the “Results” section, the prevalence of IAH is given during ICU stay and an incidence for 24 hours and 72 hours (I guess cumulative) but when it comes to mortality among those with IAH versus those without, TWO p-values (one for Mean IAP and Max IAP) are presented but p-values are NOT meaningful if not associated with variables they refer to. Moreover, the definition provided for IAH is not based on both Mean and Max IAP, reason why one should be used in the analysis and results. Although statistics used to compare those IAP in terms of mortality, there should rather have been a comparison of means or medians of IAP between survivors and non-survivors.

3) Core manuscript:

- The manuscript is somehow equilibrated but the introduction seems to be a bit lengthy with 7 paragraphs owing to unnecessary details in the last paragraph that should rather fit in the discussion section. There are some strengths but also major weaknesses that I opted to present sub-section by sub-section.

4) Introduction:

- There are no objectives for this study in the last paragraph of the introduction.

5) Methods:

- The subsection could be rearranged accordingly instead of starting with the ethical statement.
- The “study background” comprises rather the settings and period.
- There is no clear study design: cross-sectional? Cohort: follow up for only 72 hours is not enough for a cohort study.
- The patient assessment or procedures contains a statement on “pretested questionnaire”

but the authors do not give the interrater variability on the gathering of data/information or any further action taken to guarantee the quality of data collection between the PI and research assistants (This becomes particularly crucial when we analyze the prevalence of the IAH among the three hospitals, where H1 has the lowest while there is no statement on the description of those sites that may explain this difference. Therefore, one can think of variations in measuring the IAP between the sites).

Data management and statistical analysis:

- The sample size is calculated without any basis on the *outcome* of interest, the statistics intended for use in the analysis and the expected magnitude of effect of variables on the outcome.
- If the prevalence was the primary endpoint, the formula used may not be relevant and sample size small. Cochran formula may be more relevant than the Leslie Kish's.

It is good that the mortality was analyzed as a time to event (Kaplan Meier) but predictors of mortality in ICU are many and there should have been an adjustment of some of them to show that the IAH is really an independent predictor to mortality in ICU.

6) Results:

- There are so many tables and on page 6 of the manuscript we see 2 tables but only 1 (table 2) is numbered.
- Also table 1 and table 2 as they do both represent baseline characteristics could be combined into one table and omit the present variables that do not bring any added value to the study. The presentation of sites (H1, H2 and H3) may not have any meaning for an international reader as it is not presented anywhere that there is any difference of the three settings. Also reasons for admission can be summarized as medical or surgical/trauma; also it would be good to know exactly the time for onset of current illness prior to admission in ICU as resuscitation in wards or small hospitals without Critical Care specialists may end up with fluid overload or the opposite especially when prolonged.
- In table 2, there are statistics that are wrong in regard to comparison of numbers of patients with renal failure in IAH vs no-IAH where a Chi-square has been used while the number of cases in one category was 0. Similar remark for the table on the same page.
- Moreover, percentages presented in this table are calculated on the row instead of basing on column (we need to see the % of patient with stroke among those without IAH versus the % of stroke among those with IAH).
- The number of patients with seizures need to be reviewed as there might be an error (Table 2).
- In the table 3, the second column does not reflect % and it should be added. Also a $p=0.000$ does not exist.
- In the table 5, there is a univariate and multivariable regression analysis but it was not stated in the Methods section how variables included in the multivariable logistic (?)

regression was chosen.

- We find also variable “shock” and “need of vasopressors” in the regression model. This will definitely be an issue of collinearity that should have been checked before putting the different variables into the regression model. It is interesting to see that sepsis is an independent predictor for the IAH but one can wonder whether septic shock is not. The definition of variables used could be clearly defined in the “Methods” section. Fluid balance did not “survive” the logistic regression to stand as an independent predictor but if well defined (measurable/quantified), the results might have probably been different.
- In Table 6, the IQR needs to be revisited to show both 25th and 75th percentile as IQR instead. Also, there is no reason explained in “Methods” to present Max IAP. It should have been interesting rather to present different grades of IAH and related them to mortality in ICU.
- The comparison of LOS between the two groups may not be a good estimate as those who died have been included. Analysis of the time to event (survival analysis) is an accurate one.
- For the Kaplan Meier curves, as stated above, different other predictors may have influenced the outcome and could be considered in the adjustment. Therefore, a Cox Hazard Proportional Model could have been used.

7) Discussion:

- The authors should make a thorough discussion with inference of the impact of IAH on the bad outcome instead pairing findings from other studies without any tangible critical appraisal of those findings or the findings in this study.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Anesthesiology, Critical Care, Infectious Diseases

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.