Survival and predictors of mortality among patients admitted to the intensive care units in southern Ethiopia: A multi-center cohort study

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ABSTRACT

Background: The burden of life-threatening conditions requiring intensive care units has grown substantially in low-income countries related to an emerging pandemic, urbanization, and hospital expansion. The rate of ICU mortality varied from region to region in Ethiopia. However, the body of evidence on ICU mortality and its predictors is uncertain. This study was designed to investigate the pattern of disease and predictors of mortality in Southern Ethiopia.

Methods: After obtaining ethical clearance from the Institutional Review Board (IRB), a multi-center cohort study was conducted among three teaching referral hospital ICUs in Ethiopia from June 2018 to May 2020. Five hundred and seventeen Adult ICU patients were selected. Data were entered in Statistical Package for Social Sciences version 22 and STATA version 16 for analysis. Descriptive statistics were run to see the overall distribution of the variables. Chi-square test and odds ratio were determined to identify the association between independent and dependent variables. Multivariate analysis was conducted to control possible confounders and identify independent predictors of ICU mortality.

Results: The mean (±SD) of the patients admitted in ICU was 34.25(±5.25). The overall ICU mortality rate was 46.8%. The study identified different independent predictors of mortality. Patients with cardiac arrest were approximately 12 times more likely to die as compared to those who didn’t, AOR = 11.9(95% CI:6.1 to 23.2).

Conclusion: The overall mortality rate in ICU was very high as compared to other studies in Ethiopia as well as globally which entails a rigorous activity from different stakeholders.

1. Introduction

The modern intensive care medicine emerged during the Polio epidemics in the 1950s, which was pioneered by a Danish anesthetist, Bjorn Ibsen at the Kommune hospital of Copenhagen in 1953 [1,2].

The Intensive Care Unit (ICU) is a specially staffed, well equipped, separate, and self-contained area of a hospital dedicated to providing aggressive therapy using state-of-the-art technology and both invasive and noninvasive monitoring for critically ill and high-risk patients [3–6].

The burden of life-threatening conditions requiring management in the intensive care unit has grown substantially in the last couple of decades in low and middle-income countries because of an emerging pandemic, motorization, urbanization, and hospital expansion [7–12]. However, the advancement of ICU care is very limited in these countries due to the high cost of infrastructure, training medical staff, failure to incorporate international guidelines for evidence-based care, and availing medical supplies [9,11,13–16].

Intensive care unit comprises only 10% of hospital bed but it costs more than 30% of acute hospital care which is equivalent to 20% of the hospital budget and this cost becomes higher in a patient with a severe critical illness which hinders the low resource setting to establish...
Critical ill patients are admitted to ICU for some reasons including but not limited to respiratory failure, severe infectious diseases, multiple trauma and shock, myocardial infarction, heart failure, renal failure, poisoning, postoperative care, and therapeutic [18–37]. Evidence showed that the incidence of ICU admission ranged from 1 to 54% globally [17,35,37–40]. The cause of ICU admission is not consistent across the globe and the majority of available evidence showed that cardiovascular and respiratory disorders were the commonest causes of admission in middle and high-income countries accounting for 27–41% of admission [17,35,37–40] while trauma and postoperative care were the main reasons for ICU admission in low-income countries which varied from 10 to 50% [6,37,38,41].

Evidence revealed that the outcomes of patients in ICU is greatly related to different factors including but not limited to the pattern of diseases, the severity of the disease, infrastructure, trained medical staff, nursing care, medical supplies, age of patient, presence of comorbidities and multiorgan failure, pre-hospital and emergency care trauma score, mechanical ventilation, length of ICU stay, complications in ICU, dissemination of antimicrobial-resistant microorganisms and inappropriate or suboptimal use of antibiotics [6,9,18,24–28,30,34,36,37,40–48].

The global prevalence of mortality in ICU roughly ranges from 9 to 61%. An international study recruiting 13,796 participants from Africa, Asia, America, Europe, and Oceania revealed that the prevalence of mortality in ICU was 18.2% [49]. Other evidence from Sub-Saharan Africa showed that mortality in ICU was ranged from 27% to 61% [38,41,50,51]. A systematic review and meta-analysis by Vincent et al. showed that ICU mortality related to appropriate Biochemical tests. 

The prevalence of mortality in ICU is very high in the low-income country which is as high as 61% as compared to developed countries which varied from 9 to 18% [28,38,41,50,51,53]. The rate of ICU mortality in Ethiopia varied from region to region ranging from 27 to 38% [4,6,28,32,46,53]. However, the pattern of disease and predictors of mortality in the Southern part of Ethiopia is not well investigated. This multicenter observational study was designed to investigate the pattern of disease and predictors of mortality in selected Southern Ethiopia ICUs.

2. Materials and methods

2.1. Protocol and registration

This study was conducted in compliance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies and strengthening the reporting of cohort studies in surgery (STROCSS) [54,55]. The study was registered retrospectively in research registry with Unique Identifier Number (UIN:: researchregistry6641) and available at: https://www.researchregistry.com/browse-the-registry#home/

2.2. Study design and setting

This is a multi-center retrospective Cohort study conducted in three teaching and referral hospitals in Southern Ethiopia; namely, X University referral hospital, Y University referral hospital, and Z referral hospital from June 20, 2018, to May 20, 2020. These teaching and referral hospital are administered by the Federal Ministry of health and education of Ethiopia. The ICUs are providing a similar level of care with almost similar staff profiles, monitoring modalities, ICU infrastructure, medical supplies, and admission patterns. The care of patients in these ICUs is to the minimum standard because of lack of medical supplies (mechanical ventilator, integrated monitors, vasopressor/inotropes, nutritional support), lack of well-trained staff (lack of intensivist, dentition/nutritionist, physiotherapist). Besides, Y University referral hospital and Z University hospital ICUs didn’t have Computerized Tomography (CT), portable chest X-ray Machine, Spirometer, and appropriate Biochemical tests.

2.3. Eligibility

The inclusion criteria for this observational study were all adult patients who were 12 years and above admitted to ICUs of the three referral and teaching hospital during the study period. All patients with incomplete data greater than 15% were excluded. The incomplete date in less than five percent of the records was entertained with the assumption of multiple imputations.

2.4. Variables

2.4.1. Dependent variables

The dependent variables were the clinical outcomes in ICU including 30-day mortality, length of ICU stay, the incidence of cardiac arrest, and complications in ICU.

2.4.2. Independent variables

Socio-demographic characteristics (age and gender), causes of admission, presence of comorbid illness, category of admission, the vital sign at admission, intervention during ICU stay were the independent variables.

2.5. Sample size and sampling procedure

The sample size (n) was determined using a single population proportion formula with the following assumptions: level of confidence (α) was taken as 0.05; Zα/2 = 1.96, a 4.6% margin of error (d = 0.46), and proportion of mortality 46% was taken from a study conducted in Jimma University(46). Therefore, the total sample size was 524 with a 15% contingency for the non-response rate. As shown with a strobe flow diagram (Fig. 1), the total ICU admission in three centers was (N = 2129) patients. The total ICU admission in Z, Y, and X Universities were 647, 680, and 802 respectively. The study populations were taken from each ICU with a proportion allocation formula by dividing the admission in each ICU by the total admission of the three ICUs multiplied by the sample size (n = 524). Z = n1/N + n, Y = n2/N+ n, and X = n3/N+n where n1, n2, and n3 were the total admission in Z, Y, and X respectively. Then, the required number of participants were selected with systematic random sampling with a skip interval of (k = 4).

2.6. Data collection procedures

The data was collected by three trained bachelors Anesthetist with standardized questionnaire adapted from previous literature [25,32,36,41,44,49,50,56–58]. A total of 524 patient charts were recruited from 2119 patients admitted in ICU from June 20, 2018, to 2020 in three hospitals with systematic allocation proportion based on the number of patients admitted during the study period (Fig. 1).

The data extraction includes Socio-demographic characteristics (age of the patient, gender, weight, Height, BMI); Admission variables (admission category, causes of category, vital sign at admission; intervention in ICU (mechanical ventilation, vasopressor requirement); complication in ICU (cardiac arrest, infection, aspiration) and outcomes (mortality, length of ICU stay and some mechanical ventilator).

2.7. Data analysis

The data was checked, coded, and entered into Epi-info version 7.0 and imported to SPSS version 22 and STATA version 16 for analysis. Descriptive statistics were summarizing with tables and figures. The categorical variables were reported in Frequency and percentage and
the statistical difference was determined by Chi-square and Fisher exact test where appropriate. The numerical data were reported in mean ± SD for symmetric and median (Interquartile range) for asymmetric numeric data. The outlier of the data was checked with standardized residual while Shapiro Wilk tests were employed for the normality test. The multicollinearity among independent variables was checked by the Variance inflation factor and tolerance.

Association of demographic characteristics, admission category, causes of admission, and intervention in ICU, a complication in ICU and mortality in ICU was analyzed by using binary logistic regression. The Model fitness was checked using Hosmer-Lemeshow goodness of fitness test, Pseudo R2, and Pearson chi-square statistics. All Variables that were significant on bivariate analysis at a p-value less than 0.25 were taken to multivariate analysis one after the other to investigate model prediction and independent predictors of the explanatory variables. In multivariate analysis, a p-value of less than 0.05 was considered for the statistical association. The finding of this study was reported in compliance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies [54,55].

2.8. Ethical statement

This study was reviewed and approved by the Institutional Review Board (IRB) of XXXXXXX and was given a reference number (007/19-10). The study was conducted in compliance with the Helsinki declaration for observational studies. A formal letter was written to each University hospital ICU director to get permission to access the patients’ data and all the patient identifiers were kept anonymous.

3. Results

A total of 2119 patients were admitted to the three teaching referral Hospitals’ ICU from June 2018 to May 2020. Five Hundred and twenty-four patients were selected with systematic proportion allocation from three ICUs. Finally, Five hundred and seventeen were included in the analysis, and the rest seven were excluded due to incomplete data.

3.1. Admission characteristics

The mean (±SD) of the patients admitted in ICU was 34.25(±5.25). The majority of patients were in the age range of 19–39 years while the lowest was in the less than 18 years range. Among 517 patients, the majority 274(53%) were female while males accounted for 247(47%).

The majority of Admissions were from the emergency department 223(43.1%) followed by Medical ward 180(34.8%), gynecology/Obstetrics ward 50(9.7%) while the lowest were from operation theatre 47(9.1%) and surgical ward 17(3.3%). The commonest causes of ICU admissions were acute respiratory distress syndrome, Congestive heart failure, and severe pneumonia, stroke, myocardial infarction, and acute kidney injury respectively.

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The majority of patients had a respiratory rate greater than twenty breaths per minute while less than twenty-three of patients had respiratory rate less than twelve breaths per minute. Seventy percent of the patients had a pulse rate greater than a hundred beats per minute while only six percent of patients had no palpable pulse at admission. More than half 272(53.2) of patients had a GCS score of less than eight while 197(37.1%) of the patients were hypoxemic (PSO2 less than 90%) at
admission. This study identified different causes of ICU admission among 517 cohorts. The majority causes of ICU admission were Trauma 185(35.5%) followed by others 90(17.4%), ARDS 57(11%), and congestive heart failure 55(10.6%) (Table 1).

3.2. Comorbidity, intervention, and outcomes

All Patients admitted to ICU had some comorbidity. The cardiovascular disorders were the commonest comorbidity 183(35.4%) followed by others 90(17.4%), ARDS 57(11%), and congestive heart failure 55(10.6%) (Table 1).

### Table 1

| Characteristics                                               | All admissions (n = 517) | Survivors (n = 275) | Non-survivors (n = 242) | P-value |
|---------------------------------------------------------------|-------------------------|---------------------|-------------------------|---------|
| Age range (years)                                             | 102(19.7)               | 39(35.3)            | 63(64.7)                | >0.05   |
| <18                                                           | 233(45.1)               | 117(50.2)           | 116(49.8)               |         |
| 19 to 39                                                      | 182(35.2)               | 86(47.3)            | 96(52.7)                |         |
| >40                                                           | 274(53.0)               | 149(54.4)           | 125(45.6)               | >0.05   |
| Gender                                                        |                         |                     |                         |         |
| Female                                                        | 243(47.0)               | 126(51.9)           | 117(48.1)               |         |
| Male                                                          | 279(53.0)               | 123(48.1)           | 156(51.9)               |         |
| Admission vital                                              | 23(4.4)                 | 20(86.9)            | 3(13.1)                 | <0.0001** |
| sign                                                          | 119(23.0)               | 42(35.3)            | 77(64.7)                | <0.0001** |
| Respiratory rate                                              | 375(72.5)               | 180(48.0)           | 195(52.0)               | <0.0001** |
| <12                                                           | 330(63.8)               | 169(51.6)           | 161(48.4)               | <0.0001** |
| 12 to 20                                                      | 141(27.3)               | 36(25.5)            | 105(74.5)               |         |
| >20                                                           | 13(2.5)                 | 9(69.2)             | 4(30.8)                 |         |
| Pulse rate                                                    | 33(6.4)                 | 28(84.8)            | 5(15.2)                 |         |
| >100                                                          | 325(62.9)               | 184(56.0)           | 141(43.4)               |         |
| 60 to 100                                                     | 197(37.1)               | 58(29.4)            | 134(70.6)               |         |
| <60                                                           | 272(53.2)               | 184(67.6)           | 91(32.4)                |         |
| Oxygen                                                        | 196(37.9)               | 51(26.0)            | 145(74.0)               |         |
| Saturations (%)                                               | 46(8.9)                 | 7(15.2)             | 39(84.8)                |         |

### Table 2

| Characteristics                                               | All admissions (n = 517) | Survivors (n = 275) | Non-survivors (n = 242) | P-value |
|---------------------------------------------------------------|-------------------------|---------------------|-------------------------|---------|
| Comorbidities, n (%)                                          | 183(35.4)               | 97(53.0)            | 86(47.0)                | >0.05   |
| Cardiovascular disease                                        | 153(29.6)               | 79(51.6)            | 74(48.4)                |         |
| disease                                                       | 31(6.0)                 | 15(48.4)            | 16(51.6)                |         |
| Respiratory disease                                           | 59(11.4)                | 25(42.4)            | 34(57.6)                |         |
| disease                                                       | 133(25.7)               | 77(57.9)            | 56(42.1)                |         |
| Renal disease                                                 | 29(5.6)                 | 15(51.7)            | 14(48.3)                |         |
| Infectious disease                                            | 35(6.8)                 | 16(45.7)            | 19(54.3)                |         |
| disease                                                       | 27(5.2)                 | 14(51.9)            | 13(48.1)                |         |
| Neurological disease                                          | 5(1.0)                  | 3(60.0)             | 2(40.0)                 |         |
| Endocrine disease                                             | 30(5.8)                 | 15(50.0)            | 15(50.0)                |         |
| Gastrointestinal disease                                      |                         |                     |                         |         |
| Hematological disease                                         |                         |                     |                         |         |
| disease                                                       |                         |                     |                         |         |
| Rheumatic disease                                              |                         |                     |                         |         |
| Others                                                        |                         |                     |                         |         |
| Intervention                                                  | 278(53.8)               | 91(32.7)            | 187(67.3)               | <0.0001** |
| Mechanical                                                    | 185(35.8)               | 86(46.5)            | 99(53.5)                | 0.027*  |
| Ventilation                                                   | 274(53.0)               | 145(52.9)           | 129(47.1)               | >0.05   |
| Inotropes                                                     | 236(45.6)               | 123(52.1)           | 113(47.9)               | >0.05   |
| Vasopressors                                                  | 203(39.2)               | 8(40.0)             | 126(60.0)               | >0.05   |
| Fluid                                                         | 78(15.1)                | 38(48.7)            | 40(51.3)                | >0.05   |
| Blood                                                         | 9(1.7)                  | 5(55.6)             | 4(44.4)                 | >0.05   |
| Transfusion                                                   | 35(6.8)                 | 16(45.7)            | 19(54.3)                | >0.05   |
| Feeding                                                       | 324(62.7)               | 142(45.8)           | 51(56.2)                | <0.005* |
| Surgery                                                       | 248(48.0)               | 139(56.0)           | 109(44.0)               | <0.0001** |
| GIT prophylaxis                                               |                         |                     |                         |         |
| Antibiotics                                                   |                         |                     |                         |         |
| others                                                        |                         |                     |                         |         |
| Complications                                                 | 125(24.2)               | 23(18.4)            | 102(81.6)               | <0.0001** |
| Cardiac arrest                                                | 177(34.2)               | 9(52.5)             | 84(47.5)                | >0.05   |
| Anemia                                                        | 43(8.3)                 | 24(55.8)            | 19(44.2)                | >0.05   |
| Arrhythmia                                                    | 96(19.1)                | 44(44.4)            | 52(55.6)                | 0.034*  |
| Infection                                                     | 332(64.2)               | 176(53.0)           | 156(47.0)               | >0.05   |
| Hypotension                                                   | 94(18.2)                | 54(57.4)            | 40(42.6)                | >0.05   |
| Hypertension                                                  | 15(2.9)                 | 10(66.6)            | 5(33.3)                 | 0.032*  |

Note: ** very significant; *significant; ARDS: Acute Respiratory Distress Syndrome; PSO2: percutaneous oxygen saturation.
Hawassa University (38.4%) (Fig. 3).

Fig. 3: Mortality status among ICU centers in Southern Ethiopia from June 20, 2018, to May 20, 2020.

3.3. Determinants of ICU mortality

The variables showing a p-value of less than 0.25 in bivariate analysis were entered in multivariate analysis with a forward selection method as the explanatory variables were more than fifteen. The model fitness was estimated with Pearson chi-square statistics ($X^2 = 282$, DF = 9, $p = 0.0001$) and Pseudo $R^2 = 0.561$ and insignificant Hosmer–Lemeshow goodness of fit ($p = 0.412$). Fifty-six percent of the variation of ICU mortality was explained by the independent variables entered in the final regression model and the rest forty-four percent of the variation may be due to chance or other factors.

The variables that showed a significant difference in multivariate analysis were cardiac arrest, GCS score, aspiration, antibiotic use, mechanical ventilation, hypoxia, infection, and ICU length of stay. The multivariate analysis revealed that Patients who sustained cardiac arrest in ICU were approximately 12 times more likely to die as compared to those who didn’t have a cardiac arrest, OR = 11.9 (95% confidence interval (CI): 6.1 to 23.2). The Multivariate analysis also showed that patients whose GCS score less than eight were 8 times more likely to die, OR = 8.2 (95% confidence interval (CI): 2.7 to 25.5) (Table 3).

4. Discussion

This multi-center observational study revealed that the majority of patients admitted to ICU were female and younger productive age groups, 19–39 years old which are in line with other studies conducted in Sub-Saharan African countries [6,19,28,32,38,41,46]. The possible explanation for this difference in this age group in low-income countries might be due to engagement in violence, road traffic accident and relatively educated with high health-seeking behavior. On the contrary,
the rate of admission to ICU in developed nations was among older patients that might be due to a sedentary lifestyle and high prevalence of a non-communicable disease among these patients [23,27,33,35].

The commonest causes of ICU admissions in our study were cardiovascular and respiratory disorders which are comparable with studies conducted globally [2,6,20,28,32,45,48,49,52,53,58,59]. However, there are discrepancies on the causes of intensive care admission unit where studies conducted in Kenya, Tanzania, Uganda, Nigeria revealed postoperative events were the major causes of Admission [38,41,56] while studies were done from Jimma University referral hospital and Addis Ababa Black Lion hospital was due to trauma [46,53]. An international study from six continents including 10069 patients and another study from Belgium and the UK suggested that the major causes of admission were cardiovascular and respiratory disease [20,40,45]. This difference may be explained by the types of ICU, level of care of the hospital, types of study design, and socio-demographic characteristics of the population.

This study revealed that the majority of patients were hypotensive, septic, comatose, and hypoxemic with unstable vital signs which were strongly associated with 30-days ICU mortality. In our study, more than fifty percent of patients were on a mechanical ventilator and from which more than sixty percent died during follow up. This high rate of mortality in patients with mechanical ventilator may be related to a frequent power cut, improper nursing care as they were not trained formally, lack of medication, malnutrition as there was no standard nutrition supplement, and ventilator-associated complications.

The overall ICU mortality rate of this study was higher than studies done in a different region of Ethiopia such as Addis Ababa (39%), Gondar (38.7%), Jimma (37.7%), Mekelle (27%) [32,46,60,61] and other studies conducted in sub-Saharan Africa namely: Nigeria (34.6%), Uganda (40.1%), and Tanzania (41.1%) [38,41,62]. On the other hand, it is lower than studies conducted in Jimma (50.4%), National Hospital of Abuja (68.4%), and Burkina Faso 60% [63–65]. This discrepancy might be due to differences in sample size, level of ICU care, availability of medical supplies, and stratification of skilled staff.

In this study, cardiac arrest, aspiration, being on a mechanical ventilator, hypoxemia at admission, and low GCS, and the use of antibiotics and length of stay were independent predictors of mortality. This study revealed that patients who sustained cardiac arrest were approximately 12 times more likely to die as compared to those who didn’t, AOR = 11.9(95% CI: 6.1 to 23.2). This high risk of death might be related to inadequate resuscitation drugs and equipment, lack of well-trained staff in advanced cardiac life support (ACLS), inappropriate post-cardiac arrest care, and compliance with ACLS protocol.

The study also revealed that patients with aspiration were 5.6 times more likely to die, AOR = 5.6(95% CI: 1.1 to 29.4) and patients on antibiotics for a prolonged period were still 5.7 times more likely to die as compared to those who didn’t have, AOR = 5.7(95% CI: 3.2 to 10.2) which was in line with an observational and systematic review [33,47,66,67]. The possible explanation might be the rapid emergence and dissemination of antimicrobial-resistant microorganisms, administering unnecessary broad-spectrum antibiotics, and undue antibiotics for a prolonged period.

This study showed that ICU mortality was strongly associated with trauma, congestive heart failure, ARDS, and stroke which are comparable to studies conducted in Sub-Saharan African countries [2,6,46,53]. The possible explanation might be lack of Emergency medical care System (EMS) in pre-hospital, inadequate specialists, lack of well-trained ICU staffs, well-equipped integrated monitors, and drugs. Besides, the cost of ICU is very high for low and middle-income countries to establish modern well-equipped ICU because ICU requires a huge investment for training medical staff, purchasing medical supplies, and establishing ICU infrastructures.

### 4.1. Limitation of the study

This is a multi-center observational study with more than one month follow up and a relatively large sample size. However, this study is not without limitations. The nature of data handling management, unavailability of biochemical tests to determine the severity and prognostic score such as acute physiologic and chronic health evaluation (APACHE), sequential organ failure assessment (SOFA), Simplified Acute Physiology Score (SAPS) was the possible limitations.

### 4.2. Political implication

This multi-center observational study revealed that the overall mortality rate in ICU was very high as compared to other studies in Ethiopia as well as globally. The main independent predictors of mortality were traced and this entails a rigorous activity from different stakeholders. The majority of predictors could be prevented by availing emergency drugs for management of shock, cardiac arrest, aspiration, intracranial hypertension, arrhythmia, pain management, and sedation; integrative patient monitors as most of the monitors were not functional; training of ICU nurse because most of the nurses didn’t have formal intensive care training; provision of adequate calories; availing bedside tests including portable X-ray, ultrasound, and biochemical tests.
4.3. The implication for further research

It has been known that retrospective study has its limitations as some important parameters may not be available. Besides, we didn’t assess the severity and prognostic scores due to the unavailability of biochemical tests in some centers. Therefore, a multi-center prospective cohort study is in demand.

5. Conclusion

The overall ICU mortality rate was very high. The majority of independent predictors were cardiac arrest, aspiration, infection, unstable vital signs at admission, and being on a mechanical ventilator which could be minimized by implementing appropriate ICU care with a set of guidelines and protocols.

Ethics approval and consent to participate

Ethical clearance and approval were obtained from the ethical review board of the College of Health Science and Medicine.

Consent for publication

Not applicable.

Availability of data and materials

Data and material can be available where appropriate.

Registration of Research Studies

The study was registered retrospectively in research registry with Unique Identifier Number(UIN:researchregistry6641) and available at: https://www.researchregistry.com/browse-the-registry#/home/

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Declaration of competing interest

The authors declare that there are no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102318.
