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- Introduction
- Methods
- Results
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Editorial

COVID-19 remains a challenge, disrupting healthcare systems across the globe. Kenya, like many parts of the world has experienced an increase in the number of COVID-19 cases. There has been a general increase in the number of intensive care admissions for the period between April and July 2020. The exponential increase in the number of patients with hypoxemic respiratory failure has worsened our ICU strain, especially in the month of July.

During the sporadic phase of the pandemic, severely hypoxic patients or those with progressively failing respiratory function triggered an intentional low threshold for invasive ventilation. For a number of reasons, this was associated with low rates of intensive care survival. On review therefore, there has been a shift in paradigm, withholding airway instrumentation and optimizing lung function with the use of non-invasive modes of oxygen therapy.

It is inline with this that our first article makes a summary of the operating principles of non-invasive ventilation, its indications and benefits in critically ill COVID-19 patients with hypoxemic respiratory failure.

Apart from highly infectious diseases, the epidemiology of critical illness has generally changed in the last decade. Trauma has become an important cause of emergency room and intensive care strain. The use of triage scores to decide on the appropriateness of care has been explored in the second article.

Our practice of anaesthesia and critical care still borrows heavily from international protocols. The definition of brain death which has medical-legal implications must be tailor made to meet other aspects of life, the socio-cultural environment. Attempts at local protocol formulation are crucially important as explained in the third article.

The highly infectious nature of COVID-19 has led to multiple frontline healthcare worker exposures in the country, some of whom have progressed into critical illness and death. More than ever before has there been more need for adequate human resource in the healthcare space. Personal health, quality and appropriate use of protective equipment in appropriate care environment cannot be overemphasized.

On the positive aspect, the pandemic has indirectly given an impetus towards the realization of some aspects of Universal Health Coverage. Some parts of the country (Kenya) now have access to well-equipped intensive care facilities and readily available oxygen therapy. Telemedicine and internet penetration have facilitated new knowledge acquisition and sharing, adoption of new technology and a true appreciation of value of quality offered by critical care specialists and teams. The limitation in human resource capacity has come with urgent need for healthcare workforce recruitment, and equipment with appropriate skill set, mental health support to prevent clinician burnout. Significant attention to maintaining a healthy society is needed especially at this time of the world's probable worst public health crisis.

Respiratory Failure and COVID-19 P. Is Non-Invasive Ventilation an Option?

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Abstract

COVID-19 pandemic has disrupted healthcare systems with slightly over 600,000 deaths worldwide as of 30th July 2020. While majority of confirmed cases are asymptomatic or present with mild disease, about 5% are critically ill requiring intensive care support(1). Being a new disease, we hope to share our experience in managing these patients in our intensive care unit (ICU) and lessons learnt along the way. Whereas early invasive ventilation has been the norm, use of non-invasive ventilation (NIV) is gaining support with good results. To minimize risks of aerosolization, the practice of NIV in CODID-19 necessitates proper use of personal protective equipment (PPE) and negative pressure ventilation in ICU.

Introduction

COVID-19 results from infection with SARS-COV2, a novel coronavirus first isolated in Wuhan, China in December 2019 (2). Kenya, like many African countries, has seen steady rise in new infections in the last one month. As of 30th July 2020, there were 19913 confirmed cases and 325 fatalities, with a projected peak in infections in August 2020(3). More worrying is the lack of preparedness by healthcare systems in Africa which can easily be overwhelmed with a spike in the number of critically ill patients.

The WHO definition of COVID-19 critical illness includes the presence of organ dysfunction in the setting of positive reverse transcriptase PCR for SARS-COV2(4). Organ dysfunction is characterized by decline in organ function necessitating the need for therapeutic intervention e.g. mechanical ventilation for acute respiratory distress syndrome (ARDS)(4) (2). Patients with ARDS have bilateral lung opacities not fully explained by volume overload or cardiac failure.

The severity of ARDS is determined by the PaO2/FiO2 ratio. Mild ARDS is characterized by PaO2/FiO2 ratio of 200-300 mmHg. The moderate and severe forms have ratios of 100-200 mmHg and <100 mmHg respectively(5). Apart from hypoxemic respiratory failure, COVID-19 critical illness may also result from acute pulmonary embolism, acute coronary syndrome, renal failure, acute stroke and delirium(6).

NIV involves the application of positive pressure by use of tight-fitting masks, hoods or helmets as patient-ventilator interfaces. Continuous Positive Airway Pressure (CPAP) and Bi-Level Positive Airway Pressure (BiPAP are the two main modes of NIV(7)(8)(9).

CPAP delivers a constant flow of oxygen at a prescribed pressure (measured in cmH20) which remains constant throughout the ventilatory cycle. Intrinsic positive end expiratory pressure is the residual pressure preventing collapse of the alveoli and is estimated to be between 2.5 and 3 cmH2O. CPAP is usually commenced at a level (5cmH2O) that is higher than the intrinsic pressure. The application of Positive End Expiratory Pressure (PEEP) prevents alveolar collapse and increases lung volumes, leading to a reduction in pulmonary shunt fraction(9).

BiPAP involves the use of two levels of continuous positive airway pressure: Inspiratory Positive Airway Pressure (IPAP) and Expiratory Positive Airway Pressure (EPAP). IPAP settings usually range from 12 to 35cmH2O, while those of EPAP are set similar to CPAP. For adequate tidal volume to be achieved, the difference between IPAP and EPAP (driving pressure) should be at least 8cmH2O. This improves ventilation and may be useful in patients with hypercapnia e.g. COPD or COVID-19 patients with COPD (9)(10).

Use of NIV to support patients with respiratory failure caused by COVID-19 has been controversial. Recent review of data by Schunemann et al suggested that early and appropriate application of NIV reduced the need for invasive ventilation, albeit with a risk of transmission of infection to healthcare workers(11). In this series, we intend to describe 18 patients who were managed using NIV with mixed outcomes.

Methods

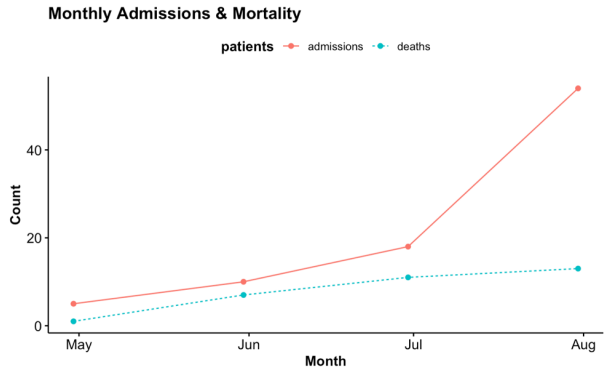
This is a case series looking at a select 18 critically ill COVID-19 patients managed at Kenyatta University Teaching Referral and Research Hospital ICU with NIV.

Results

For the period between April and July 2020, a total of 87 patients were admitted into the intensive care unit. There was a general increase in the number of monthly intensive care admissions, with an exponential phase beginning in the month of July. Out of these admissions, 32 patients died giving a mortality of rate of 36.8%.

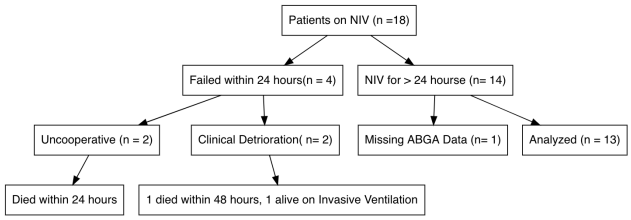
At the beginning of the pandemic, there was a low threshold for intubation which was associated with high mortality. Based on emerging data, there was a change in protocol to include NIV for patients meeting the criteria (cooperative and able to protect airway); and timely intubation for those that clinically deteriorated or became intolerant.

Figure 1: Monthly Intensive Care Admission and Mortality Trend



18 out of the 87 admissions were managed using NIV with mixed outcomes. 4 patients failed NIV within 24 hours, 3 of whom died within 2 days of ICU stay. The other patient was intubated and invasively ventilated. 3 other patients failed NIV (refractory hypoxemia and severe hypercapnia) after 24 hours of ICU stay.

Figure 2: Patient Outcomes following Initiation of NIV



Patient Characteristics

Majority of the patients on NIV were male (11/18). The mean age was 52.9 with a range 40 to 67 years. There were multiple comorbidities as shown below.

Figure 3: Table of Co-Morbidities

	Morbidity	Frequency
1	Diabetes Melitus	3
2	Hypertension	1
3	COPD	1
4	Obesity	1
5	Diabetes_Hypertension	2
6	Diabetes_HIV	1

All these patients presented with increased work of breathing and severe hypoxemia despite being on high flow oxygen via non-rebreather mask i.e. median PaO2 of 44.0 mmHg (ranging from 30 to 55 mmHg) at initial evaluation. The median PaCO2 at the time of initial evaluation was 31.0 mmHg (ranging from 17.2 to 44 mmHg), suggesting an increase in minute volume in these patients. The median pH was 7.38 with a range of 7.21 to 7.50.

2 patients failed NIV due to refractory hypoxemia. The remaining patients had a significant improvement in PaO2. The median PaO2 improved from 44 to 87 mmHg after the fourth blood gas analysis.

Figure 4: Change in PaO2 During NIV

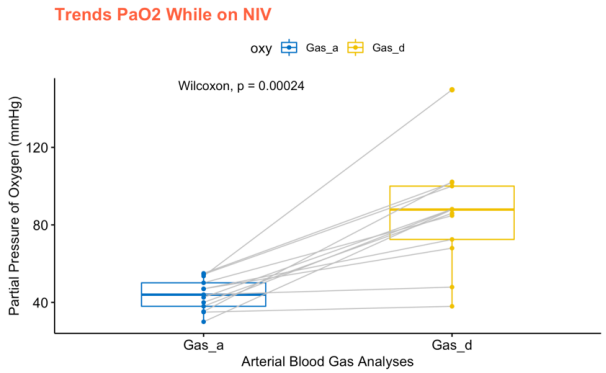
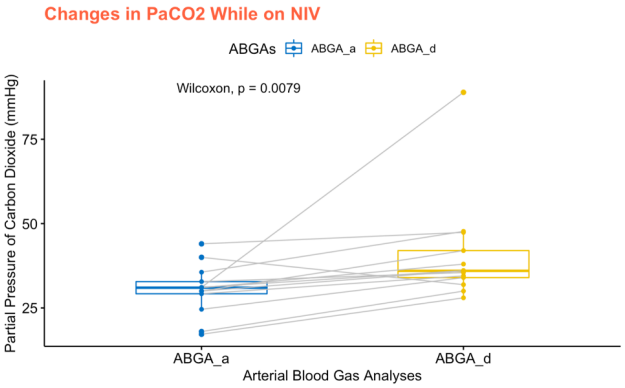


Figure 5: Change in PaCO2 During NIV



The median PaCO2 changed from 31 to 36 mmHg by the 4th blood gas analysis, suggesting a reduction in minute volume. One patient failed NIV due to extreme hypercapnia (89 mmHg) ad was intubated.

Discussion

A significant number of patients with severe COVID-19 disease develop acute respiratory distress syndrome (ARDS) and require respiratory support(11). As observed in this study, these patients usually present with worsening hypoxia without hypercapnia, increased work of breathing, confusion, altered level of consciousness and cyanosis. The median PaO2 and PaCO2 were 44 and 31 mmHg respectively. The mildly reduced PaCO2 may be related to increased respiratory drive as seen in some COVID-19 phenotypes.

During the initial outbreak, reports from China suggested that early intubation and invasive ventilation was preferable to NIV(12). At this point, NIV was associated with the potential to delay invasive ventilation. As the number of critically ill COVID-19 cases increased, ventilators became limited. This was worsened by the prolonged duration of mechanical ventilation and difficulty in weaning that is characteristic of these patients(13).

Recent evidence has shown NIV to have a more significant and positive role than initially thought (8)(13)(14). Early use of Continuous Positive Airway Pressure (CPAP) may prevent deterioration and reduce the need for invasive ventilation (8) (15). Positive pressure reduces the work of breathing and improves oxygenation by reducing intrapulmonary shunting. In severe COVID-19, initial CPAP settings have been suggested to be as high as 10 cmH2O and 100% oxygen(15) (12).

As is the protocol in our unit, NIV involves the application of a tight face mask or a hood as the interface. Patients must therefore be conscious, able to initiate their own breaths and protect their airway (14). Contraindication to NIV therefore includes failure to meet the above criteria. It is evident from this study that 4 of these patients did not meet the criteria for NIV. They were either uncooperative or had severe impairment in gas exchange making them unsuitable for NIV ab initio.

NIV may not reverse hypoxemia in all patients presenting with severe COVID-19. In some patients, NIV may temporarily improve oxygenation and work of breathing. In others, it does not change natural disease progression and is not a replacement for intubation and invasive ventilation. One of the patients in this series rapidly progressed into a cytokine storm that eventually led to death despite conversion to invasive ventilation.

Apart from monitoring the work of breathing and patient comfort during NIV, arterial blood gas analyses are necessary to evaluate the effect of this intervention. In this series, 3 patients failed NIV i.e. two with refractory hypoxemia and one with severe hypercapnia.

As described in this study, the practice of NIV involves the use of a strict criteria for patient selection, appropriate patient care environment and use of personal protective equipment. The need for both clinical and biochemical monitoring requires enhancement in human resource.

Conclusion

NIV is one of the modes of respiratory support that can be applied in management of critically ill COVID-19 patients. If well selected, majority of the patients on NIV will improve their baseline oxygenation indices and work of breathing (reduced minute volume). In absence of clinical trials to look at the effectiveness of NIV in critically ill COVID-19 patients, case series like this one will continue to add to the existing evidence of benefits of NIV in this pandemic.

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Utility Of Triage Early Warning Scores In The Care Of Critically Ill Surgical Patients At Kenyatta National Hospital

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Abstract

Background

Critical illness is a life-threatening condition involving one or more organ systems resulting in significant morbidity or mortality. Critical illness related mortality is estimated to be at 8-18%; and is preceded by a period of physiological deterioration. Early Warning Score tools have been employed to capture this period of clinical decline. The limited use of such tools in KNH general wards could lead to sub-optimal adherence to clinical pathways among trauma patients.

Objectives

Broadly, the objective was to establish the appropriateness of care level amongst critically ill surgical patients using the triage early warning score in KNH. Specifically, we intended to identify critically ill surgical patients using the triage early warning score tool in KNH A&E, establish a relationship between the triage early warning score and outcome of critically ill surgical patients after 72 hours of follow up; and determine the odds ratio of adverse outcomes using the triage early warning scores at KNH.

Methods

This was a longitudinal observational study involving 168 critically ill surgical patients who were followed up for 72 hours following recruitment. 4 hourly vitals, decisions regarding intervention, level of care and clinical outcomes were recorded. A relationship between the TEWS and clinical outcomes was established using logistic regression.

Results

The study showed that patients with high TEWS (7 and above) were at increased risk of ICU admission and death.

Introduction

Data on burden of critical illness in Africa is limited. Studies from developed countries revealed an ICU mortality rate 8-18%.[1] Delay in recognizing critical illness, paucity of clinical pathways, high critical illness severity scores at admission were identified as independent predictors of mortality.[2, 3]

Various tools were invented to capture early patient deterioration and aid in activation of prompt care. The earliest known tools were the early warning scores (EWS) from which modifications were made into modified early warning score (MEWS), triage early warning score (TEWS), national early warning score (NEWS) among others.

These warning scores are based on a track and trigger system whereby patients' vitals are recorded; and scores given for each derangement. Once the total score exceeds critical value, appropriate action is taken.

The Modified Early Warning Score

This is tool is used to detect early patient deterioration based on physiological parameters that are measured during a patient's ward stay. Vital signs e.g. heart rate, blood pressure, respiratory rate, oxygen saturation, temperature, level of consciousness as well as urine output (for catheterized patients) are scored from 0 to 3.

The total score ranges from 0 for patients with no abnormalities to a maximum of 15 for very sick patients. Various studies showed that a total score of > 5 was associated with a higher morbidity and mortality, prolonged hospital and ICU stay.[4,5, 6]

Table 1: Modified Early Warning Score

Physiological Parameter	**3**	**2**	**1**	**0**	**1**	**2**	**3**
Respiratory Rate		Less than 9		9-14	15-20	21-29	>29
Heart Rate		<41	41-50	51-100	101-110	111-129	>129
Systolic Blood Pressure	<71	71-80	81-100	101-199		>199	
Temperature		<35oC	35.1-36oC	36.1-38.10C	38.1-38.5oC	> 38.6oC	
Nuerologic State				Alert	Reacts to Voice	Reacts to Pain	Unresponsive
TOTAL							

The Triage Early Warning Score (TEWS)

This is a component of the South African Triage Scale, which was validated in KNH in 2017. It is currently in use at the KNH emergency room for detection and prioritization of patients.[7]

TEWS was modified from MEWS by adding a trauma and mobility component. Most trauma patients had previously been well, hence a large physiological reserve leading to late recognition of critical deterioration unlike in MEWS which mainly captured medical patients.

The TEWS was validated in a South African Hospital 2014. It was found that patients with TEWS >7 had significantly worse outcomes than those with lower scores. An average TEWS of 9.5 was associated with mortality; while that of 8.2 was associated with ICU admission.[8]

Table 2: Triage Early Warning Score

	3	2	1	0	1	2	3
Mobility				Walking	With help	Stretcher/immobile	
Respiratory Rate		Less than 9		9-14	15-20	21-29	>29
Heart Rate		<41	41-50	51-100	101-110	111-129	>129
Systolic Blood Pressure	<71	71-80	81-100	101-199		>199	
Temperature		Cold or < 35oC		35-38.40C		Hot or > 38.4oC	
AVPU				Alert	Reacts to Voice	Reacts to Pain	Unresponsive
Trauma				NO	YES		
TOTAL							

Study Justification

Critical care in Kenya faces a significant strain of 0.29 ICU beds per 100, 000 population. At KNH, ICU beds comprise 1.8% of the total inpatient capacity, against the WHO recommendation of 10-20%.

The mortality rate in trauma patients is significantly high in KNH ICU. This may be attributed to late recognition of critical illness in the wards. This translates to admission to ICU of patients that have severe morbidity with high risk of mortality.

Similarly, in the general wards there exists no tool to identify patients at risk of deterioration hence delayed escalation of care for such patients, as compared to the A&E where they are captured early and action instituted.

The study aimed at finding out whether the TEWS would be a useful tool in the identification and care of critically ill surgical patients presenting to the accidents and emergency department of KNH.

Methodology

Study Design

This was a longitudinal observational study involving critically ill surgical patients between the months of February 2019 to April 2019. The case definition of a critically ill surgical patient was a TEWS of >5.

Study Site

The study was carried out at the accident and emergency department and surgical wards of Kenyatta National Hospital.

Kenyatta National Hospital is an 1800 bed tertiary care facility, the largest public hospital in east Africa. It has 50 wards, with 10 wards catering for surgical patients. At the time of the study, there were 3 intensive care units, 20 outpatient clinics, 24 operating theatres, and 2 accident and emergency departments (one for paediatric and the other for adult mixed trauma and medical emergencies).

The adult accident and emergency department received between 32000 and 62000 patients per year, with a monthly average of around 4000 patients. Out of these, 20000-22000 patients are admitted to the wards per annum.

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Study Population

The study was carried out on critically ill adult surgical patients presenting to the KNH accident and emergency department with a TEWS > 5. Patients that had purely neuro-traumatic causes of target scores were excluded from the study, because a low Glasgow Coma Scale increased the TEWS by 3 points leading to sampling bias.

Sample Size

Sample size was calculated using the (Daniel, 1999) formula, and a sample size of 165 was arrived at as below;

n = (Z^2 x P(1-P))/d^2
Where,
n = Desired sample size
Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)
P = expected true proportion (estimated at 12.1%, from a retrospective observational study conducted by Naidoo D.K. et al (2014), at the Accident and Emergency Unit of Addington Hospital, KwaZulu Natal, South Africa; looking at assessing the effectiveness in identifying patients at risk of early deterioration to enable timely medical intervention using the TEWS, found 12.1% of patients had a TEWS category (high) ≥ 7.)
d = desired precision (0.05)
n = (⟦ 1.96^2 x 0.121(1-0.121)) / ⟦ 0.05 ⟧ ^2 ≈165

Data Collection

Convenience sampling was done whereby all patients fulfilling the inclusion criteria were recruited until the desired sample size was reached. Data was collected using serialized questionnaire which was filled out by trained research assistants. The vital signs taken and recorded every 4 hours over a period of 72 hours. This was used to compute the 4 hourly Triage Early Warning Scores.

Blood pressure was measured using an automatic oscillotonometric arm blood pressure machine. The cuffs were sized to cover 40% of the upper arm circumference, and 80% of the upper arm length. Automated clinical thermometer was used for temperature measurement, and a wristwatch timer was used to count the respiratory and pulse rate. The sternal rub was used to elicit response to pain in patients who are not responsive to verbal stimulation as well as touch.

Patients flagged as critically ill on scoring 5 and above using the TEWS were followed up and had the TEWS chart filled during the 72 hour-of follow up. The highest recorded TEWS score was used for data tabulation.

The outcomes of interests were the level of care accorded to the patients, and clinical outcomes after 72 hours of hospital stay.

Data Analysis

Data was collected using a pretested questionnaire and entered into excel spreadsheets. Data cleaning and analyzed with RStudioVersion 1.3.959© 2009-2020, PBC. Continuous data was analyzed and presented as means and density plots. Categorical data was also analyzed and presented as frequencies and proportions. Logistic regression was used to assess the relationship between the triage early warning score and patient outcomes at 72 hours. The results were considered significant at $p < 0.05$. Where appropriate, tables and pie charts were used to display certain characteristics.

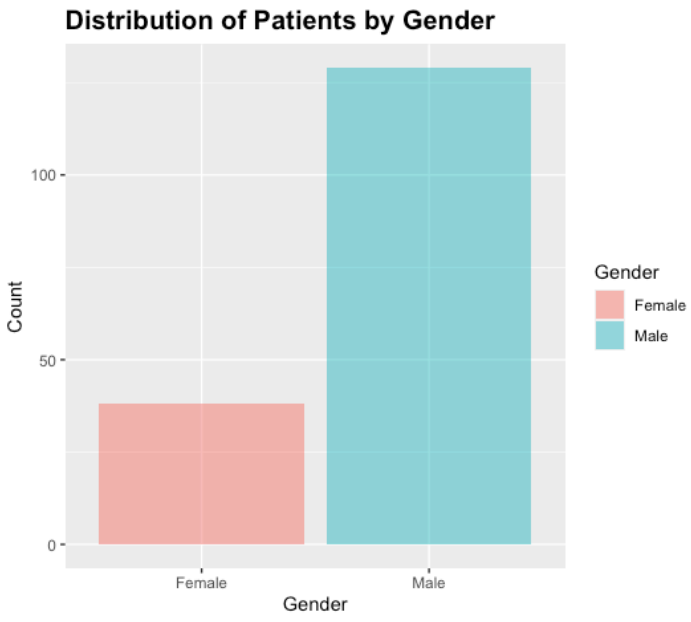
Ethical Consideration

The study was approved and registered (P664/09/2018) by the Kenyatta National Hospital/University of Nairobi Ethical and Research Committee and KNH administration. An informed consent was obtained for each eligible subject.

Results

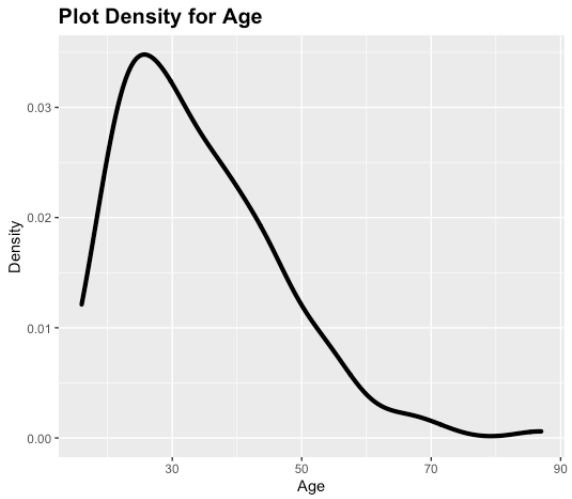
A total of one hundred and sixty-seven patients were recruited, majority of whom were male (129), consisting 77.24% of the sample size.

Figure 1: Distribution of Age by Gender



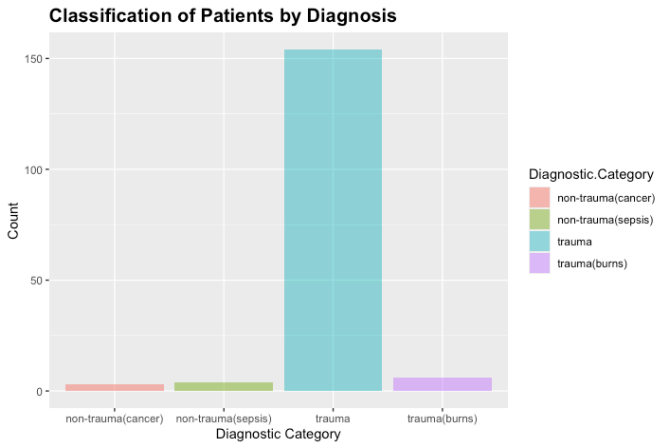
The youngest and oldest patients were 16 and 87 years old respectively, with a mean of 34.13 years. 50% of the subjects were aged 31 years and younger. .

Figure 2: Density Plot for Age



Of the cases presenting to the accident and emergency, 92.2% of them had suffered trauma. Other diagnoses were categorized as shown.

Figure 3: Diagnostic Categories



In the presentation due to trauma, most of the patients had fractures involving the limbs as well as pelvis and spinal vertebrae. They were followed by patients that had injuries involving more than one organ system (polytrauma).

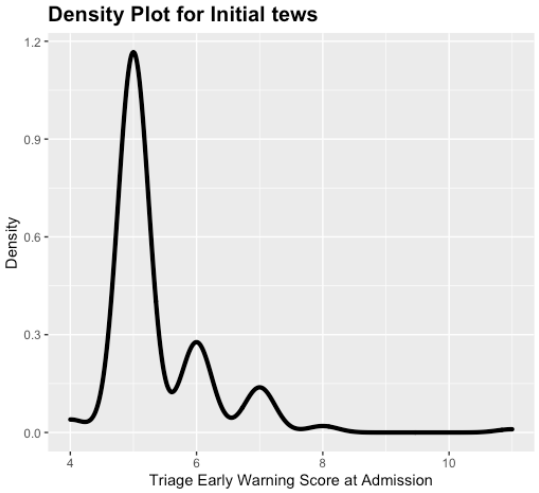
Table 3: Trauma Categories

Trauma Type	Frequency (%)
Fractures	68.98
Polytrauma	13.29
Burns	5.69
Soft tissue injury	7.59
Abdominal injury	2.53
Chest injuries	1.89
Total	**100%**

Out of the four patients that presented with malignancies, 2 needed tube thoracostomies for pleural effusion drainage, one needed emergency tracheostomy due to upper airway obstruction from cancer of the thyroid, and one had tracheostomy granulomas for otolaryngology review. Another four patients presented with sepsis (2 with peritonitis and 2 with cellulitis).

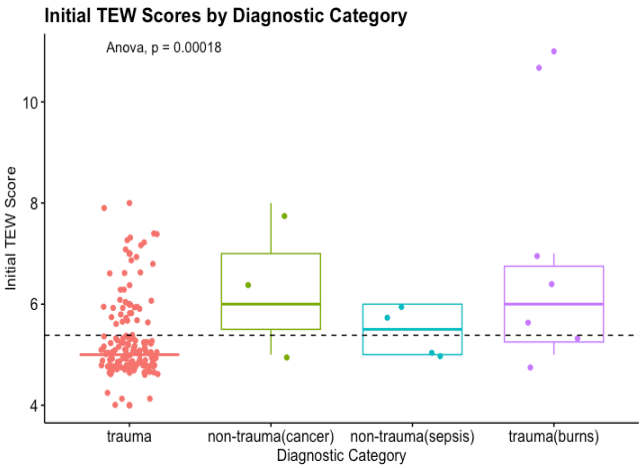
The most common score at initial evaluation was 5 which accounted for 118 patients (70.7%), followed by a score of 6 (28 patients), score of 7 (11 patients), score of 4 (4 patients), score of 8 (2 patients) and finally a score of 11 (1 patient). No patient had a score of 9 or 10. Majority of the patients had a score below 7 and accounted for 89.8%, while 10.8% of the study population had a score of 7 and above.

Figure 4: Density Plot for TEWS on Initial Evaluation



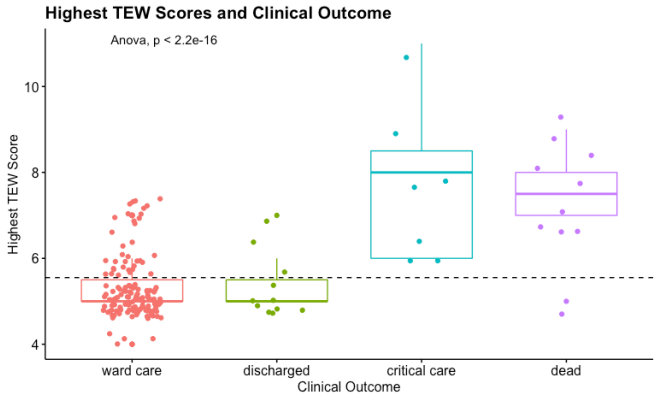
The mean TEWS at initial evaluation was 5.38. Patients with burns had the highest mean TEW score (6.67), followed by cancer patients (6.33), septic patients (5.5) and trauma patients (5.31) in descending order (p = 0.00018).

Figure 5: Comparison of Mean Initial TEWS amongst the various Diagnostic Categories



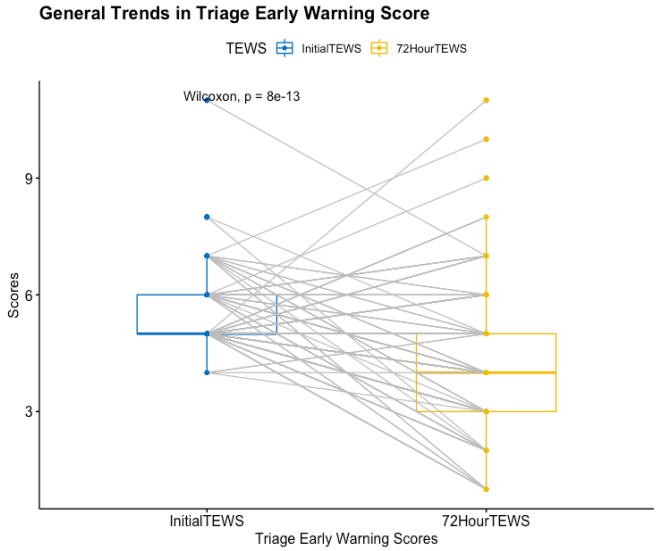
The mean highest TEWS recorded during the 72-hour follow up was 5.55. Patients in critical care had the highest mean highest TEWS (7.71), followed by those who died (7.5). Discharged and ward patients had mean highest TEWS of 5.36 and 5.32 respectively ($p < 0.05$).

Figure 6: Highest TEWS and Clinical Outcome at 72 hours



Various interventions like fluid resuscitation and surgical operations were employed to improve the clinical status of individual patients. There was a clinically significant reduction in the mean TEW score after 72 hours (4.18) from an initial TEW score of 5.38 ($p < 0.05$).

Figure 7: General Trends in Triage Early Warning Score



The odds for having a bad outcome (death or critical care admission) as calculated using logistic regression was found to be 7.708 times for each unit rise in the TEWS score, as shown below in table.

Table 5: Direct Logistic Regression for Highest TEWS and Bad Outcome

						OR 95% C.I.	
	B	**S.E.**	**Wald**	**P value**	**OR**	**Lower**	**Upper**
TEWS	2.042	.406	25.337	<0.001	7.708	3.480	17.073
Constant	-14.861	2.732	29.582	<0.001	.000		

Discussion

This study was done with the aim of establishing the utility of triage early warning score in the management of critically ill surgical patients at KNH. The patients were recruited from accident and emergency department and followed up for 72 hours.

Various studies have demonstrated that patients with MEWS or TEWS scores of > 5 are at increased risk of bad outcomes, such as critical illness, prolonged hospital stay and death. This was the basis for using the baseline score of > 5 as a criterion for inclusion into the study.

The TEWS is a modification of the MEWS. Trauma and mobility components were added to the MEWS. The trauma component is given 1 point while immobility is given 2 points on the TEWS. This would help to capture trauma patients who would have been missed due to subtle deterioration as a result their large physiological reserve.

Majority of the cases presenting to KNH A&E were due to trauma, with fractures involving the limbs, spine and pelvis. The findings were similar to those of a study on epidemiology and outcomes of injuries in Kenya.[9] Most of the trauma was due to road traffic accidents and falls from heights. This reflects on the burden of trauma, which according to the WHO, contributes to 90% of injury related deaths in low income countries.

A study in KNH showed that up to 48.8% of admissions through the accident and emergency department into surgical wards were due to trauma. The most commonly affected age group was 15-44 years, and this was reflected in our study, whereby most of the patients were male, with a mean age was 34.13 years. According to the global burden of trauma and injuries, males are more than 3 times likely to suffer non-intentional injuries such as road traffic accidents and falls.[10]

The average scores in the patients with adverse outcomes was higher than in those without adverse outcomes. Patients requiring intensive care had mean highest TEW score of 7.71, compared to 7.5 in those who died. On the other hand, patients who were admitted to the wards or discharged on initial evaluation had scored of 5.32 and 5.36 respectively. The average scores for patients that were admitted to ICU seemed higher because their number was slightly smaller (7) as compared to those that died (11).

A study done by Naidoo et al to evaluate the TEWS in an urban accident and emergency center showed that patients who had bad outcomes had significantly higher average TEWS. They found that the average TEWS for patients that died was 9.5 and 8.2 for those that were admitted to ICU (p value 0.032).[8] This was also reflected in a study by Tian et al where they found that higher scores were independent predictors of mortality. In this study, patients with TEWS of < 9 had a mortality rate of 0.98% compared to 80% among patients with TEWS of > 14. The average TEWS was significantly high at 7.05 ± 2.38 for those patients that were admitted to ICU.[11] In a Turkish study, Gorkhan et al demonstrated that average TEWS for patients that died were significantly higher at 10.6 ± 2.3 versus scores of 2.7 ± 2.3 for those that survived. [12] In this study, high TEWS (>7) were associated with poor outcomes.

Using direct logistic regression, it was established that the odds ratio for a bad outcome (death or ICU admission) was 7.7 times for each unit increase in TEWS, compared to 2.14 in the study by Tian et al. [11] This may be attributed to their large study population (456) versus 168 in our study. Since the TEWS is derived from the Modified Early Warning score (MEWS), Subbe et al found that a MEWS of 5 and above were associated with poor outcomes, with significantly increased risk for mortality with an odds ratio of 5.4.[4,5]

Conclusion

ICU strain and the burden of trauma pose a significant challenge at KNH. Based on our findings, the TEWS is a sensitive tool for predicting risk for unplanned ICU admission and death. Timely identification and action for patients at risk of deterioration using the TEWS may reduce adverse events and outcomes.

However, since the TEWS is a modification of the Modified Early Warning Score, it may over-triage patients, due to addition of the immobility component.

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The Complexity of Brain Death Diagnosis in Pediatrics: Guidelines and Potential Hurdles

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Abstract

The diagnosis of brain death poses a challenging clinical situation to the attending physician. This situation is even more difficult in paediatrics. Internationally, early defined guidelines were not specific to children, necessitating modification and constant review. Currently, formal local guidelines on brain death criteria in Kenya are lacking, requiring referral to international protocols. Unfortunately, most have been developed and tested in resource rich settings. Therefore, fulfilling all the diagnostic criteria may not always be feasible in our environment. This prompts the need for development of locally applicable protocols, for uniform determination of brain death, as it has significant medical, legal, cultural and ethical implications.

This discussion highlights the development of international brain death diagnosis criteria for children, hurdles posed in the paediatric age bracket and potential pitfalls of a hurried diagnosis. It furthermore seeks to draw attention to possible limitations of current modalities of testing.

Introduction

The definition of brain death has evolved both legally as well as medically, and has been redefined over the last 60 years by various international bodies. Cultural, ethical, religious and regional disparities have led to wide variations in attitudes towards brain death. Brain death definitions vary globally. For instance, the whole brain death concept is accepted in Australia, New Zealand and the United States of America. On the other hand, the United Kingdom, Canada and India have adopted the brainstem definition of death: "death by neurological criteria" [1-4].

The triad of apnea, absent brainstem reflexes and coma in a patient with an acute and irreversible neurological insult prompts consideration of brain death and further evaluation is necessary. Advancements in critical care have made it possible to artificially support life, even in the presence of irreparable neurologic damage [5]. These scarce and costly resources may be better allocated to patients with reversible pathologies. Therefore, meticulous care must be taken in interpreting clinical signs, diagnosing and confirming brain death.

Discussion and Literature Review

An acute neurological insult triggers a vicious cycle of cerebral oedema, raised intracranial pressure and decreased cerebral blood flow. This eventually culminates in cerebral ischemia and infarction if uncorrected. In paediatrics, brain death commonly occurs following severe traumatic brain injury, cerebrovascular accidents as in patients with sickle cell anaemia or direct damage due to tumours and central nervous system infections. Global ischemic injury following shock, cardiac arrest or severe respiratory failure may also occur. Rare causes include cellular dysoxia for example in cyanide poisoning and acute toxic neuronal injury such as in hepatic failure and other metabolic disorders [5].

Confirmation of brain death in children poses a greater hurdle as compared to adults, as the developing, immature paediatric brain may be resilient to certain external stresses and injury. This is especially true in infants. There is also a possibility for neuroplastic modelling [5].

Assessment of brainstem functions may have varying results in the young brain, due to progressive development. Shemie et al recognized that the paediatric brain is immature and development continues up to atleast two years of age [6], while others report it continues beyond the first decade of life [5].

Kohrman and Spivack described a 3-month-old infant who met the criteria for brain death diagnosis, however partial brainstem function was regained [7]. This prompts caution in assuming irreversible brain function in children.

Furthermore, the 'resilience model of recovery' plays a role in regaining certain cognitive function following a cerebral insult, as evidenced by Anderson et al in paediatric stroke [8]. The open fontanelles in infancy may also assist to maintain intracerebral pressure within normal ranges during an insult and hence limit cerebral damage [9].

Evolution of brain death diagnosis

The early definitions of brain death were not specific to children. The first documented report of cessation of brain function was in 1959, by Mollaret and Goulon. They described "le coma dépassé" (irretrievable coma): a state more severe than coma, with loss of motor activity, sensation, consciousness and vegetative functions [10]. In 1967 The American Electroencephalographic Society stated features of an irreversible coma included electrocerebral silence with complete unresponsiveness, absent cephalic reflexes, apnea and the inability to maintain circulation without artificial support [11].

A year later, in 1968 the Ad Hoc Committee of the Harvard Medical School released criteria for determining brain death. However, the recommendations did not contain any special considerations with regard to age. Signs of brain death included "irreversible coma," with absent reflexes, a flat EEG, absent movements, breathing and responses to external stimuli [12].

The American Neurological Association reviewed the Harvard criteria in 1975. They reported the criteria was inappropriate for children under five years, as evidence suggested that the immature neurological system could recover from prolonged periods of electrocerebral silence. This was based on a case report by Green and Lauber in 1972, on a five-year-old comatose patient with severe hepatic failure on mechanical ventilation. The child was reported to have been unresponsive to external stimuli, had an absent pupillary reflex and a flat EEG. However, the following day, spontaneous movement and withdrawal to noxious stimuli was noted, as well as waveform activity on the EEG.

They further discussed a case of a six-week-old infant admitted with seizures and apneic episodes who exhibited clinical features of brain death. However, on the following day of admission, EEG activity was noted, with spontaneous movement of the limbs and a few days later he began making spontaneous breaths [13].

In 1981 the Uniform Determination of Death Act was produced in the United States of America, to fulfill the objective of having a national definition of brain death. Death was concluded to have occurred with the irreversible cessation of respiratory and circulatory functions or the irreversible cessation of all functions of the entire brain in addition to the brain stem. However, it was noted that the clinician should be wary when applying this criteria in patients younger than five years and again no age specific guidelines were outlined [14].

Almost thirty years after the early descriptions of brain death concepts, the first document which considered paediatric brain death specifically was published by the Task Force for Determination of Brain Death in Children in 1987. In terms of history, of importance was to exclude reversible conditions that may be contributing to the patient's status. Physical examination findings included coexistent apnea and coma, loss of consciousness and volitional activity, and absent brainstem functions. For neonates and infants atleast two separate EEG tests were recommended in order to evaluate existence of brain activity, while for children older than one year, an EEG was not required [15].

The Academy of Medical Royal Colleges in 2008 stated consciousness and an intact breathing capacity as essential characteristics of life, and their irreversible loss therefore equates to death. However, the utility of this criteria in infants less than two months old was questioned due to lack of evidence in this population. [1]

Notably, Kenya currently lacks formal guidelines on brain death diagnosis, and therefore physicians must utilize international protocols to aid in diagnosis.

Current Guidelines

Although global practices vary, the guidelines issued by The Society of Critical Care Medicine and the American Academy of Paediatrics in 2011 have been widely adopted in paediatric brain death evaluation. Brain death is described as "a clinical diagnosis based on the absence of neurologic function with a known diagnosis that has resulted in an irreversible coma." Coma and apnoea must coexist to diagnose brain death. [1,16,17]

Determination of brain death is made on clinical grounds. Certain prerequisites must be met prior to conducting the evaluation. The evaluation examines brainstem reflexes and the apnea test. Ancillary tests are conducted to evaluate cerebral blood flow and cerebral electrical activity, in situations where sections of the clinical examination and/or the apnea test are not feasible. The examination is performed by atleast two consultants on two separate occasions, at predefined set intervals. Death is pronounced after the second examination [16].

Timing of Examination

The timing of the first examination is counted either from birth, time from a successful resuscitation following cardiac arrest or other neurologic insults. For neonates aged between 37 gestational weeks to 30 days old, the examination is conducted at 24 hours. For children between 31 days to 18 years old, the examination is first performed at 12 hours.

Neonates in clinical hypothermia are given a longer observation time, as drug metabolism is retarded and will interfere with brain stem reflexes interpretation. If residual drug effects are still present in a patient, the examination is deferred for more than 24 hours [16].

The following conditions are required prior to examination: [16]

- Exclusion of reversible causes of coma.
- Hemodynamic stability with normal arterial or mean systolic pressure for age.
- A core body temperature of more than 35 °C (hypothermia is a neurologic depressant).
- No existing metabolic and electrolyte derangements.
- No residual effects of neuromuscular blockers and discontinuation of sedatives, opioids, barbiturates, antiepileptics, anaesthetic agents (allowing appropriate time for drug elimination based on individual drug pharmacokinetics) and absence of alcohol in the circulation.

Important features in examination include: [16]

- Complete loss of consciousness, vocalization and volitional activity.
- Confirmation of flaccid tone by passive motion of the limbs and observation for induced or spontaneous movements.
- Application of noxious stimuli in the cranial nerve distribution (condylomandibular and deep supraorbital pressure), all limbs (nail bed pressure) and the trunk (sternal rub), observing for any responses.

Examination of brainstem reflexes: [16]

REFLEX	AFFERENT CRANIAL NERVE	EFFERENT CRANIAL NERVE
Oculomotor	II	III
Corneal	V	VII
Facial/ Bulbar	V	VII
Oculovestibular	VIII	III, VI
Oculocephalic *	VIII	III, VI
Gag **	IX	X
Cough – tracheal	X	***

* Not recommended, as is a weak reflex and also a risk of exacerbating cervical spine trauma.

** Use the rooting/suckling reflex in neonates.

*** Efferent is the phrenic nerve, and hence cannot be assessed in high cervical cord injury.

Apnea test: Conducted if all the above reflexes are absent. If there is no respiratory effort despite a rise in PaCO2 ≥ 60mHg or ≥ 20mmHg rise from baseline or after 10 minutes, the test is indicative of brain death [16].

In circumstances where the above tests cannot be performed, such as in head or facial trauma and cervical spine injury, ancillary tests are done. They include an EEG, radionuclide tests or four-vessel cerebral angiography. Transcranial doppler ultrasound, CT angiography and MRI angiography are not validated as ancillary tests. Notably, ancillary tests are less accurate in young infants and brainstem reflexes may also not be well developed. When conducting the apnea test in this population, bradycardia may also occur before development of hypercapnia. [16]

In 2015, The Royal College of Paediatrics and Child health provided additional recommendations specifically for infants aged from 37 weeks corrected gestation (post-menstrual) to 2 months (post-term) of age. Previous guidelines had excluded infants in this age group due to a lack of evidence for establishing a criterion as noted previously. The preconditions defined were similar to the 2011 conditions discussed above. It was stated that death by neurologic criteria may be applied to neonates from thirty-seven weeks gestation to two months of age, however with caution especially with the apnea test (may require a stronger hypercapnic stimulus) due to the immature respiratory system. It was further noted that ancillary tests do not play a role in aiding diagnosing brain death in this age group. [17]

Controversies in brain death diagnosis

Despite the above criteria for diagnosing brain death, uncertainty remains about the validity of certain aspects of these tests [18]. This uncertainty is even more profound in children, due to their immature neurologic system, which may lead to false-positive results. [5]

Motor reflexes may not reflect the integrity of higher neurologic functions.[18]

Edlow et al and Fernández – Espejo et al demonstrated latent awareness can exist in an injured brain, despite the absence of motor responses to external stimuli [19,20]. Further Edlow demonstrated that stimuli applied during MRI provides evidence of consciousness that may not be apparent on bedside examination [19]. Karakatsanis also concluded that the diagnosis of brain death is not reliable when cognition is dissociated from behavioral motor responses [21]. It was further suggested that cranial nerves carry efferent fibres to skeletal muscles and hence these motor reflexes cannot be used to evaluate the presence of higher brain functions. Moreover, autonomic, thermoregulatory and neuroendocrine functions may have the potential to recover after brief cessation [22,23].

Drawbacks of the apnea test

The basis of the apnea test is to evaluate irreversible injury to the medullary respiratory centres. However, this may not always be the case. Wijdicks and Pfeifer demonstrated that 60% of brain dead patients who recorded a positive apnea test, had a normal medulla at autopsy [24]. Both Saposnik et al and Wijdicks et al reported that 50% of patients declared brain dead still had spontaneous movements and motor responses to noxious stimuli [25,26]. Termsarasab et al demonstrated that the disconnection of the spinal cord from supraspinal centres led to motor responses to stimuli and spontaneous movements, and also a positive apnea test, which may be unrelated to the integrity of the medullary respiratory centres [27]. Furthermore, the spinal cord, spinal nerve or respiratory muscle injury can record a false positive apnea test despite normal respiratory centres, leading to a false declaration of brain death [28]. Others have concluded that an insufficient rise in carbon dioxide levels and hyperoxia may cause a false positive apnea test [29-31].

Possibility of recovery of conscious awareness via neurogenesis and neuroplasticity [18].

It has been demonstrated that an acute reduction or cessation of global cerebral perfusion is the final common pathway leading to the development of the clinical features of brain death [32]. However, Walker demonstrated that only 40% of brain dead patients displayed features of ischemic brain necrosis at autopsy, while 10% had a normal brain [33]. Wijdicks and Pfeifer also showed normal or minimal ischemic features on the cerebrum in approximately 40% of brain dead patients, with corresponding figures of 63% for the midbrain, 59% for the pons and 60% for the medulla [34]. Coimbra suggested that a global

ischemic penumbra explains the absent neuronal ischemia and necrosis in brain death [35]. However neuronal electrical silence does not necessarily equate to irreversible neuronal damage [36]. The parahippocampal gyrus and the hippocampal body retain functional responses to neurotransmitters in vitro [37]. This raises the important concern of the chance of possibly reversing damage in other brain regions over time. Sharma et al demonstrated that neuroplasticity and neural remodeling can regenerate neural connections and restore function in severe brain injury [38]. Regeneration of corticothalamic pathways contributes to the recovery of conscious awareness [39]. Huang and Thibaut showed that neuroplasticity leads to recovery of consciousness and motor functions in the injured brain. Persisting neuronal transmitters play a role in recovery of consciousness in patients declared brain dead [40,41]. This possibility of neurogenesis is especially important in children who have suffered neurological insults.

Conclusion

The diagnosis of brain death poses a challenging scenario especially in children, due to a window of uncertainty attributable to the complexity of the developing nervous system. There is no universally adopted definition and the diagnosis of brain death has several cultural and legal implications, and therefore must not be made in a haste. To avoid this a certain diagnosis of brain death is required, and as such, the development of locally applicable guidelines.

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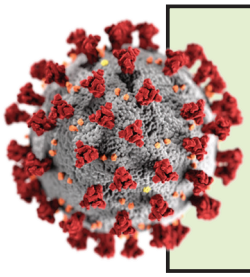

IDENTIFICATION OF MODERATE AND SEVERE COVID-19 DISEASE AFTER CONFIRMATION OF TESTS

Conversion Tables

1. Estimating PaO_2 from a given SO_2

SO_2 (%)	PaO_2 (mmHg)
80	44
81	45
82	46
83	47
84	49
85	50
86	52
87	53
88	55
89	57
90	60
91	62
92	65
93	69
94	73
95	79
96	86
97	96
98	112
99	145

2. Estimating FiO_2

Method	O_2 flow (l/min)	Estimated FiO_2 (%)
Nasel cannula	1	24
	2	28
	3	32
	4	36
	5	40
	6	44
Nasopharyngeal catheter	4	40
	5	50
	6	60
Face mask	5	40
	6-7	50
	7-8	60
Face mask with reservoir	6	60
	7	70
	8	80
	9	90
	10	95

ARDS is when $PAO_2/Fi0_2$ = 300 or less.

The lower the figure the more severe the disease.

MODERATE COVID-19 INFECTION: COURSE AND MANAGEMENT

- Feeling worse, tachypnoec i.e breathing fast and shallow but no shortness of breath.
- Fever unrelenting.
- Nausea and diarrhoea (if present), persists.
- Unable to get out of bed for natural calls.

MODERATE COVID-19 INFECTION: MANAGEMENT

- Requires oxygen supplementation by high flow non rebreather oxygen mask and associated monitoring using pulse oximetry and continuous ECG.

SEVERE COVID-19 INFECTION: COURSE AND MANAGEMENT

- Should call for an ambulance to take them to hospital, (discourage relatives / friends from doing this).
- Should be picked by a team wearing PPE's.
- Typically require 2 - 8 litres of Oxygen per minute via nasal prongs / simple face mask / (hood for children if available).
- NIV, Nasal CPAP not recommended because of aerosolization of viral particles.
- Have difficulty mobilizing thick secretions.
- Often require volume resuscitation, but do not overdo this.
- CXR shows typical picture of diffuse infiltrates.
- CT Scan shows typical picture.
- Can last for hours to days before progressing or waning.
- Oxygen requirements start increasing to above 8 litres/ minute to keep saturations above 92%.
- Coughing requires increasing effort and secretions worsening.
- Patient more anxious and subjective shortness of breath.
- Worsening CXR. (CCSK recommends to avoid repeating CXR/CT's at this time, but to make decisions based on the clinical picture).
- Period last hours to a few days (non-defined so far).
- Arrange transfer to ICU for controlled Rapid Sequence Intubation (RSI) with an appropriate sized endotracheal tube.

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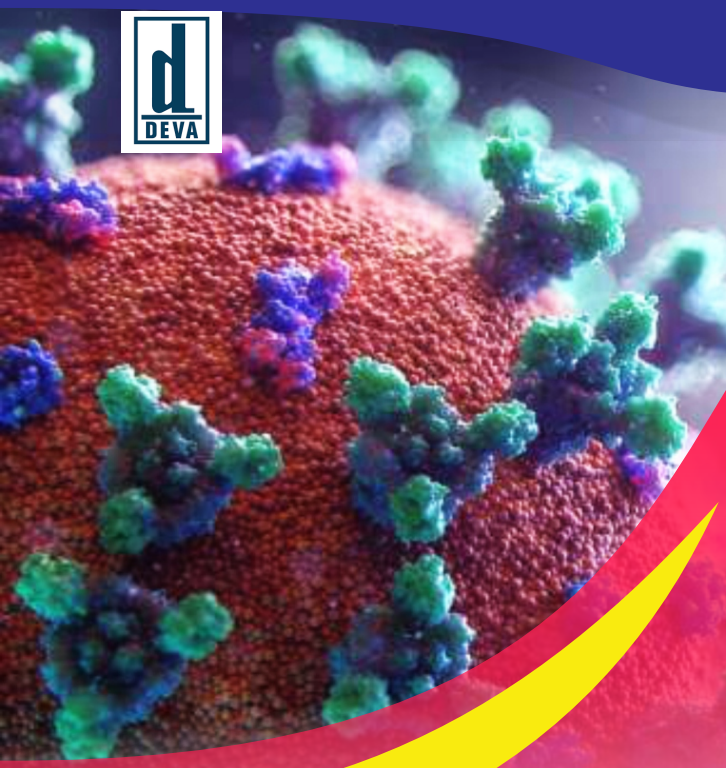

Azitro 500mg
Arythromicin

Azithromycin for COVID-19

An extract from an article :
"Azithromycin for COVID-19 : More Than Just an Antimicrobial?"
by Nathalie Bleyzac[1] · Sylvain Goutelle[1,2] · Laurent Bourguignon[1,2] · Michel Tod[1,2]

COVID-19 infection due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a major public health issue worldwide. No vaccines or drugs for prevention and treatment have been approved so far, except Remdesivir.

Immunomodulating drugs could provide a benefit in the treatment of COVID-19. Drugs with the most relevant immunomodulatory profile remain to be found. We believe the antibacterial macrolide **Azithromycin** has a special and interesting profile in this search for drug therapy for COVID-19. We discuss below the arguments for this claim[3].

Azithromycin has significant antiviral properties. The article from Andreani et al. also reported a significant antiviral effect of Azithromycin alone on SARS-CoV-2[14].

Azithromycin appears to decrease the virus entry into cells [2, 8]. In addition, it can enhance the immune response against viruses by several actions. It up-regulates the production of type I and III interferons (especially interferon-β and interferon-λ), and genes involved in virus recognition such as MDA5 and RIG-I [7, 12, 13, 15, 16]. These mechanisms are universally involved in the innate response against infectious agents, and potentially against SARS-CoV-2.

SARS-CoV-2 has been shown to exacerbate the inflammatory response of its host, leading to serious damage of lung interstitial tissue. By contrast, **Azithromycin** shows an interesting immunomodulatory profile by inhibiting several cytokines involved in COVID-19 severe respiratory syndrome. Indeed, **Azithromycin** regulates and/or decreases the production of IL-1β, IL-6, IL-8, IL-10, IL-12, and IFN-α [10, 22, 23]

Azithromycin could allow a sufficient memory T-cell count to be maintained and a better immunization.

Based on is its antibacterial effect, **Azithromycin** offers interesting options in treatment of SARS-CoV-2 and prevention of bacterial co-infections. **Azithromycin** is a possible treatment for Prevotella infections and decreases Prevotella-induced inflammation.

To conclude, there are several arguments supporting a potential effectiveness of **Azithromycin** in SARS-CoV-2 infection, including its antiviral activity and immunomodulatory effects.

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