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ORIGINAL RESEARCH

Opinions of doctors working in South African critical care units regarding unconsented testing and empirical treatment of HIV-positive patients in ICU

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Background: There exist a limited number of studies demonstrating the benefit of initiating anti-retroviral agents (ARVs) for the treatment of human immunodeficiency virus (HIV) in the critical care setting. However, there are physiological, practical, and ethical arguments against making HIV testing and initiation of ARVs routine practice.
Methods: A self-administered, cross-sectional survey of healthcare professionals was conducted with data collected using a questionnaire distributed to delegates of the Critical Care Society of South Africa (CCSSA) 2016 Congress, and members of the society.
Results: There were 101 respondents. Eight per cent would not consider testing a critically ill patient for HIV (status previously unknown), largely because they considered this unethical. Sixty-nine per cent would consider commencing ARVs in a patient newly-diagnosed with HIV during an inter-current critical illness. The factor most likely to guide them towards this was severity of illness. In general, the greatest concerns focused around biological/medical issues. However, those clinicians who would not consider initiation of ARVs were more likely than those who would, to be concerned about psychosocial issues.
Conclusion: Although the majority of clinicians would consider initiation of ARVs acutely in critically ill patients, it is apparent that the clinical decision-making around this matter is complex. Advocacy is needed to further clarify relevant ethical and legal dilemmas, and in the interim consultative and collaborative care is encouraged.

Keywords: critical care, anti-retroviral agents, HIV, survey, South Africa

Introduction

Human immunodeficiency virus (HIV) is a global epidemic, and South Africa (SA) is its epicentre.[1] The model of management of HIV has shifted from damage control and palliation in the 1980s, to chronic disease modification in the present day. The cornerstone of this progress has been anti-retroviral therapy (ART), and despite a limited choice of anti-retrovirals (ARVs) available in the public sector in South Africa, there has been an increase in the longevity and quality of life of HIV-positive patients.[2]

It has not been established to date whether initiation of ARVs in critically ill patients admitted to an intensive care unit (ICU) favours good clinical outcomes or not. Regarding the possible benefits of early initiation of ARVs, two retrospective studies, and one prospective randomised controlled trial suggest benefits. These benefits are summarised as follows:

1. Out of 58 patients admitted to ICU with *Pneumocystis carinii (sic)* pneumonia, the twelve who either continued with ARVs, or had ARVs initiated in ICU, exhibited a lower mortality than those not receiving ART.[3]
2. The six-month mortality in 278 HIV-infected patients admitted to ICU, was lower in those patients who were given ART, especially if this was introduced within the first four days of admission.[4]
3. In 282 patients randomised to receive either early or deferred ART in the management of AIDS-related opportunistic infections (some of whom were treated in ICU), the "early ART" arm experienced less AIDS progression and death.[5]

Many ARVs are considered to be toxic, both as single agents, and in combination (with many potential pharmacokinetic and pharmacodynamic interactions). Also, the first few weeks and months following ART initiation have associated risks (for example, immune reconstitution inflammatory syndrome, risk of poor compliance, and non-retention in care). Other uncertainties around initiating ARVs in critically ill patients include two important factors:

1. The higher likelihood of enteral malabsorption, in the face of poor availability of parenteral ARVs.
2. The confounding effect of critical illness on the implications of a low CD4 count for the urgency with which ARVs should be initiated.

Knowledge of a patient's HIV status can result in a change in the clinical assessment and management, regardless of the risk-benefit balance of acute ART initiation, and the reason for admission to an ICU. For example, antimicrobial cover for a severe pneumonia may be broadened beyond typical community-acquired organisms, to include sulfamethoxazole-trimethoprim for *Pneumocystis jirovecii*, if a patient is HIV-infected.

In defining its guiding principles, the South African National Department of Health's National HIV Testing Services (HTS) Policy refers to the Constitution of the Republic and the importance of protecting human rights, with informed consent being a key part of the counselling and testing process. In the specific case of people unable to make a decision due to unconsciousness, the spouse, next-of-kin, clinician or clinical manager (in the specific order listed) are authorised to give informed consent for clinically indicated HIV testing (termed proxy consent for testing).[6] Disclosure of the result to the provider of proxy consent is mentioned in cases of irreversible neurocognitive impairment, but there is no further guidance about disclosure of the result of an acutely unwell patient, or in the event of the death of the patient. In these situations, one can anticipate an ethical dilemma, due to ongoing stigmatisation of HIV.

To circumvent this, it is generally recognised that clinicians do practise unconsented ("silent") HIV testing, aiming to perform formal counselling and testing with informed consent once the patient regains capacity. Specifically in the domain of critical care, in a survey the results of which were published in 2016, most of the 24 respondents preferred unconsented testing over surrogate/proxy consent for testing by next-of-kin, which was regarded as neither reliable, nor acceptable.[7]

In summary, there is a lack of evidence and policy supported by clinicians to guide everyday clinical practice. In the face of this uncertainty there exist many concerns, thus making it a contentious issue.[8] This survey seeks to determine expert opinion of intensivists regarding initiation of ARVs in ICU.

Methods

Design

This was a self-administered, cross-sectional survey of healthcare professionals working in critical care units in South Africa. Ethical approval was obtained from the uMgungundlovu Health Ethics Review Board of the KwaZulu-Natal Department of Health, in Pietermaritzburg, South Africa (Ref: UHERB160501). The study was endorsed by the Critical Care Society of Southern Africa (CCSSA, https://www.criticalcare.org.za).

Study population

The population of interest was defined as doctors working in South African critical care units, having gained the sub-specialty Certificate in Critical Care (offered by the Colleges of Medicine of South Africa), or those that regularly care for patients in critical care units (excluding interns and community-service medical officers).

Questionnaire administration

The population was sampled by approaching delegates of the 2016 CCSSA Congress, and asking them to complete a paper survey. Sixty-seven responses were submitted, which fell short of the target of 100. Thus, the survey was transcribed onto an online platform (Google Forms), and the link to the online survey was distributed to heads of South African academic critical care departments (for dissemination to their workforce), and to CCSSA members via the society email list. Consent was requested prior to proceeding with the survey (regardless of the platform), and participants could enter a draw for a voucher.

Data analyses

Data were analysed using descriptive statistics – responses were summarised using percentages and medians. Where appropriate, associations between participants' characteristics and their responses were analysed by chi-squared/Fisher's exact tests or univariate logistic regression (to calculate odds ratios) using STATA software version 12.1 (Stata Statistical Software: Release 12.1 (2012). StataCorp LLC, 4905 Lakeway Drive, College Station, TX, USA). A p-value of < 0.05 was used for defining statistical significance.

Results

A total of 101 responses was received (67 from the paper format, 34 submitted online). The characteristics of the respondents are summarised in Table I.

Table I: Demographic profile of participants

Variable		Value
Age	Range (median)	27–69 (43)
Gender	♂ : ♀	57 : 44
Number of years spent working in critical care	Range (median)	0.33–38 (10)
> 20 hours/week in ICU	Full-time : part-time	87 : 12
Level of career	Specialist : non-specialist	92 : 6

As critical care is a sub-specialty, the base specialty of respondents was determined (Figure 1), the commonest being Anaesthesia.

Most respondents worked in mixed critical care units, looking after predominantly surgical and medical patients.

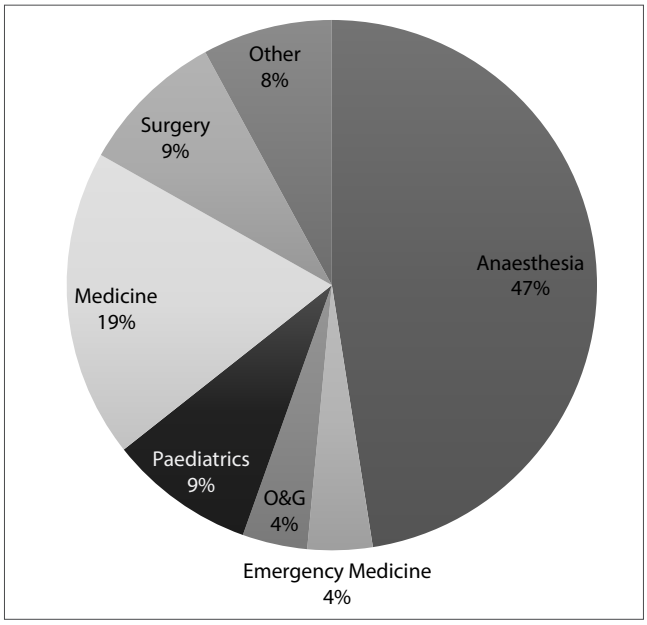

Figure 1: Base specialty of participants

Testing for and treating HIV in ICU

A scenario was posed involving an adult patient with a previously unknown status admitted to ICU, having an HIV test done without their consent (due to having impaired cognitive competence), and the test being positive. It was asked if, once enteral tolerance had been established, respondents would consider commencing ARVs in ICU.

The majority (69%) said they would, whilst 23% elected not to consider commencing ARVs. The remaining 8% who chose to opt-out (on the basis that they were not comfortable with unconsented HIV testing) were asked about their opinion of unconsented HIV testing. Forty-five per cent of respondents considered the act unethical, and 27% of respondents cited uncertainty of how to go about carrying out a test without the patient's consent.

Perceived concerns about initiating ARVs in ICU: "What do you consider to be the greatest problem about acute ARV initiation in critically ill patients?"

Responses are shown in Table II. Overall, the perceived main concerns with commencing ARVs were immune reconstitution inflammatory syndrome (36% of respondents), unpredictable enteral absorption in critical illness (35%) and ARV toxicity confusing/worsening the clinical picture (26%). Amongst respondents who were open to acute initiation of ARVs in ICU, compared to respondents who did not initiate ARVs, there was significantly less concern that "Lack of patient counselling prior to ARV initiation infringes on patients' rights" and "Lack of patient counselling prior to ARV initiation makes continuation of ARVs on discharge from hospital unlikely". None of the other potential concerns were significantly associated with choice to initiate ARVs.

Factors influencing ARV initiation in ICU

Further examining the opinions of those who would potentially initiate ARVs acutely, the majority of respondents (38%) chose the severity of the current illness as the factor which would most likely guide them to consider acute initiation. Conversely, the most commonly-cited reason (32%) for steering away from acute initiation of ARVs, was a lack of complete enteral tolerance (Figures 2 and 3).

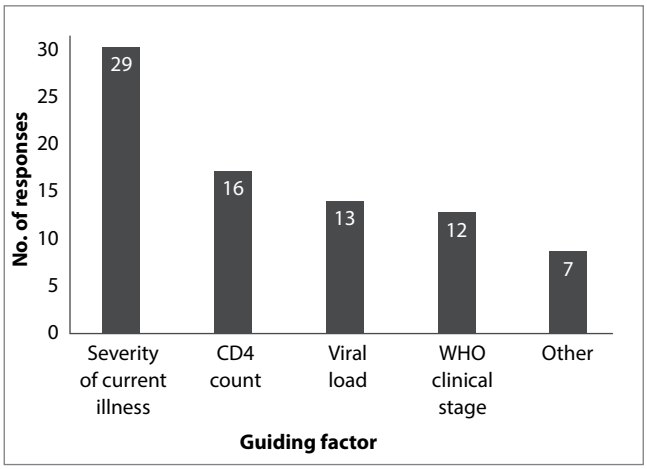

Figure 2: The factor most likely to prompt initiation of ARVs in ICU

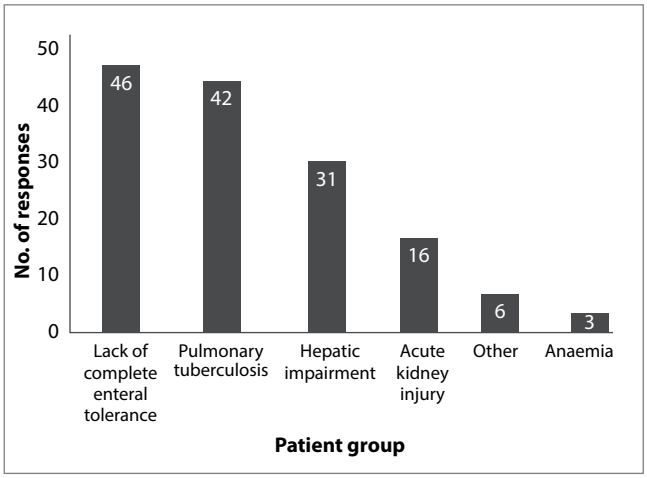

Figure 3: Factors making initiation of ARVs less likely

Clinical decision-making

Of those clinicians considering initiating ARVs in ICU, most did not have any postgraduate qualification specific to HIV

Table II: Perceived concerns about initiating ARVs in ICU

Concern	Would consider ARVs *n* (%)	Would not consider ARVs *n* (%)	Odds ratio of those who would consider ARVs holding a particular concern in comparison with those who would not consider ARVs (*p*-value)
ARV toxicity confusing/worsening the clinical picture	15 (21.4)	10 (37.0)	2.157 (0.119)
Immune reconstitution inflammatory syndrome	28 (40.0)	7 (25.9)	0.525 (0.2)
Unpredictable enteral absorption in critical illness	26 (37.1)	8 (29.6)	0.713 (0.488)
Lack of patient counselling prior to ARV initiation infringes on patients' rights	3 (4.3)	5 (18.5)	**0.197 (0.035)**
Lack of patient counselling prior to ARV initiation makes continuation of ARVs on discharge from hospital unlikely	9 (12.9)	10 (37.0)	**0.251 (0.01)**
Other	2 (2.9)	2 (7.4)	2.72 (0.33)

management. Only 7% would choose to do so alone, mostly choosing the "first-line" regimen (as defined by the National Consolidated Guidelines) if no contraindications existed.[9] For those choosing to consult another clinician, 78% said they would consult with an infectious diseases or HIV specialist prior to commencing ARVs in a critically ill patient. Ten per cent each chose another intensivist or an internal medicine specialist.

Overall, there was no significant association between the formal postgraduate training of clinicians, and the likelihood of them consulting another clinician when considering acute initiation of ARVs (Fisher's exact test, $p = 0.011$). Although most Fellows of the Colleges of Physicians or Surgeons said they would initiate ARVs only after consulting with a colleague, more initiated ARVs alone than was true of other clinicians, but this difference was only statistically significant for surgeons (OR of consulting 0.07 compared to anaesthetists; $p = 0.04$).

HIV stigma: "Do you think that the stigma associated with HIV is changing in the patient population you are managing?"

Fifty-seven per cent of respondents thought it was changing, whilst 31% thought not, and 12% were unsure. There was no significant association between the age of respondent, or number of years spent in critical care, and the opinion regarding the changing nature of HIV stigma ($Chi^2 = 10.9$, $p = 0.37$, and $Chi^2 = 7.7$, $p = 0.66$ respectively).

Discussion

Testing for and treating HIV in ICU

The main findings of this study are that the majority of intensivists working in South Africa think that unconsented testing for HIV in a patient with impaired capacity to consent is acceptable, and that a positive HIV test warrants consideration of acute treatment, in consultation with experts. This consideration is mostly informed by a balanced assessment of the severity of the inter-current illness, and short/medium-term medical concerns about immune reconstitution inflammatory syndrome, and unpredictable enteral tolerance (see "*Perceived concerns…*" and "*Factors influencing…*" below).

For those who were uncomfortable with unconsented HIV testing, the ethics of the act was the greatest concern. The main focus in the relevant literature is the potential for an assault on patient autonomy (a patient's readiness to be tested, and to accept ARVs as a life-long treatment) and breach of confidentiality (social/psychological impact on the patient of disclosure to the family). It has also been stated that HIV exceptionalism is likely perpetuated by the human rights protections created around HIV infection (and not extended to hepatitis B and C, two other blood-borne viruses), and paradoxically undermines human rights – with greater public education, some of this may change.[7]

Another trend noted was the lack of confidence in navigating the ethical and legal dilemmas around testing for HIV without informed consent; as pointed out in Singh's aforementioned study, at the moment, if guidelines are to be followed, there is a duality between autonomy and beneficence.[7]

There is a paucity of data around the knowledge, attitudes and practices of intensivists around HIV in the South African critical care environment. Singh found that 83% of a sample of 24 intensivists in South Africa considered unconsented testing for HIV to be ethical.[7] This compares with 95% of our sample of 101, who did not highlight any ethical barriers to performing or acting on an unconsented HIV test.

When looking at why intensivists choose to deviate from the ethical/legal framework suggested by the relevant guidelines, Singh found that 83% of respondents felt that the guidelines were no longer relevant to critically ill patients, and nearly 92% of respondents felt that the current guidelines did not serve the best interests of these patients, with a strong significant association between these two questions.[11]

In a survey describing the attitudes of critical care specialists around ethical dilemmas relating to HIV, Naidoo posed two scenarios and asked the participants whether they believed urgent initiation of ARVs would influence ICU outcome and general prognosis.[12] Scenarios dealing with an elderly HIV-infected patient with multiple co-morbidities and a young HIV-infected patient were posed. Fifty-four per cent and 74% of intensivists supported urgent initiation of ARVs for these patients respectively. Statistically significant associations were demonstrated between supporting this practice, and admitting the patient to the ICU with the first patient, and disclosing the patient's HIV status to the spouse with the second patient.

Perceived concerns about initiating ARVs in ICU

For those not open to acute initiation of ARVs in ICU, their concerns were more likely to focus on the effect of inadequate counselling on compliance and long-term retention in care (with subsequent development of resistance, which has individual and public health implications), and the individual rights of the patient.

Factors influencing ARV initiation in ICU

The role of the severity of the inter-current illness in guiding management speaks to empirical management, and individualised care, rather than being prompted by a laboratory test result (e.g. CD4 count). The significance of the CD4 cell count is not clear in critically ill patients.[13] Previous treatment guidelines reserved ARVs for patients who had started to become immunocompromised with HIV, as evidenced by a low CD4 cell count (or a late-stage defining illness). Most recently, the South African National Department of Health has implemented Universal Test and Treat guidelines, which mean that all people living with HIV are considered for lifelong ARVs, irrespective of CD4 count.[14] These guidelines do continue to encourage 'fast-tracking' initiation of ARVs in patients with a lower CD4 cell count.

Clinical decision-making

As mentioned previously, there exist a limited amount of retrospective and prospective data, which demonstrate potential benefit of early initiation of ARVs in ICU. However, the clinical characteristics of the patients involved in these trials are

not those of most patients treated in the South African critical care setting, who, in the main, rather than being admitted to an ICU with an AIDS-defining condition, need intensive care for management of an acute illness unrelated to HIV (e.g. acute pancreatitis, polytrauma), and are unwittingly infected with HIV.[15]

Of note, The South African HIV Clinicians' Society's Adult ART guidelines discourage initiation of ARVs in ICU, in the setting of acute critical illness or injury.[16] However, should the patient be admitted to ICU for prolonged periods, and multi-organ dysfunction has resolved, consideration of initiation is encouraged.

This study highlights a disparity between opinions of the experts in the disease (HIV clinicians, who discourage the practice), and the experts in the care of the critically ill patient (intensivists, who would consider the practice).

HIV stigma

Most respondents felt that stigma associated with HIV is changing in the patient population. This is consistent with the evidence, which characterises a complex relationship between the scale-up of ARVs and the nature of stigma experienced by people living with HIV.[10] We tested the hypothesis that those who had been in clinical practice for a longer period of time (and thus had experienced the pre-ARV era), would have a different perception of the change in stigma, but no significant association was found.

Limitations

This was the first study of its type in South Africa and as such there were no similar validated questionnaires. The survey was tested and revised following review by several specialists but formal validation through a pilot study was not performed. In this regard, multiple limitations were retrospectively noted.

A limitation general to questionnaire surveys includes the fact that responses describing opinions might not reflect practice. This is particularly relevant when considering that the two survey platforms could have introduced bias specific to each platform (e.g. respondents submitting a paper survey regarding a legally and ethically contentious issue in person, may answer differently to a respondent using an anonymous online platform). Statistical analysis of differences in responses between the two platforms was not conducted.

Another acknowledged limitation of questionnaire surveys is that the sample is not necessarily representative of the population that is defined as of interest. The size and characteristics of the population (doctors working in South African critical care units) is not known. Thus representativeness cannot be commented on and the results cannot be generalised to all South African intensivists.

Looking specifically at the survey platforms, neither platform prevented submission of multiple responses by one participant. The paper platform did not implement branching logic, thus some respondents chose multiple answers in a single best answer scenario, or answered questions that were not necessarily relevant to them. However, anecdotally, these responses suggested that those who are uncomfortable with unconsented HIV testing, would consider initiating ARVs in ICU (presumably if the test were implemented in line with ethical/legal standards), and those who proceeded with an unconsented test were not necessarily comfortable with the act.

The purely quantitative methodology did not suit in-depth analysis of some variables. Although most clinicians felt that HIV stigma was changing, the nature of that change was not characterised. Likewise, respondents may have had a different understanding of the phrase "severity of the intercurrent illness" as their main stimulus for considering acute initiation of ARVs.

Conclusion

The majority of intensivists believe that unconsented testing for HIV is acceptable, and that a positive HIV test warrants consideration of acute treatment, in consultation with experts. This suggests that HIV is a disease which needs to be considered in the holistic management of the critically ill patient. Current literature reveals consultation would likely discourage acute commencement. Although this paper serves as a reminder of this, we suggest that the consultative practice alluded to by the results should continue, pending more robust evidence.

In addition, we suggest that legal and ethical clarity about HIV testing in incompetent critically ill patients should be advocated for, especially when HIV may be a contributor to the illness.

Competing interests

The authors have no competing interests to declare.

Acknowledgements/financial support/conflicts of interest

We declare that we have no financial or personal relationship(s), which may have inappropriately influenced us in writing this paper.

Ethics

Ethics approval was obtained from the uMgungundlovu Health Ethics Review Board of the KwaZulu-Natal Department of Health, in Pietermaritzburg, South Africa (Ref: UHERB160501).

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