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Clinical Presentation and Outcomes of COVID-19 Patients Supplemented with Approved Herbal Preparations in Tanzania: A Cohort Study

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Abstract

Introduction: During the COVID-19 pandemic, there was no known specific treatment for coronavirus Disease. Because of this, different countries and institutions have used different regimens to manage disease symptoms. In Tanzania, well-known and long-used herbal preparations believed to have antiviral activities were used as supplements to standard care for COVID-19 management. This study assessed the clinical presentation and outcomes of hospitalized COVID-19 patients receiving standard care plus herbal preparations in Tanzania.

Methods: An observational cohort study was conducted between February and May 2021 at 12 health facilities. Sociodemographic information, clinical presentation, past medical history, baseline, and follow-up laboratory records were documented. Each study participant was followed up for 14 days from enrolment.

Results: 285 participants were enrolled; their mean age was 59.2 ± 16.5 years, and males constituted 56% of the study participants. Nearly 33% were aged 50 years and above. The majority (72%) reported having at least one form of co-morbidities (raised blood pressure, diabetes mellitus, asthma, Chronic Obstructive Pulmonary Diseases (COPD) and other forms of heart problems apart from hypertension). More than 60% of the study participants reported to have used at least one form of locally available herbal preparations. Symptoms and signs reported at enrolment subsided relatively faster among those supplemented with herbal preparations than among their counterparts. PCR results of nearly 66% of the study participants had converted to PCR negative at different rates by day 7 (61 vs 78%) and by day 14 (64.3% vs 36.4%) among herbal and non-herbal users, respectively. Overall, proportionally mortality was higher among those who used standard care alone (23.3% vs 16.9%) compared to those supplemented with herbal preparations.

Conclusion: The use of herbal preparations in addition to standard care treatment showed a positive effect in subsiding signs and symptoms and decreasing mortality among COVID-19 patients. The findings from this study call for further research, especially clinical trials, to ascertain these findings.

Keywords: Herbal preparations, COVID-19 outcome, Clinical presentation

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Introduction

The emergence of the COVID-19 pandemic stretched the health systems globally. Despite different efforts employed by scientists, there were no established medications for the management of COVID-19, except for some of the approved COVID-19 vaccines (WHO, 2020a)

In many communities, herbal preparations are the main contributor to primary health care, building on longstanding cultural acceptability in its use (Agyei-Baffour et al., 2017), with anecdotal estimates of 80–90% of rural populations relying on plant-based herbal preparations for the management of the different health conditions (Attah et al., 2021). Several researchers around the globe have evaluated different herbal extracts and identified phytoconstituents with different mechanisms of action against the viral infection. Hence, herbal preparations were believed to alleviate the effects of infectious diseases such as severe acute respiratory syndrome-related coronavirus (SARS-CoV-2) and improve the clinical conditions of COVID-19 patients (Musoke et al., 2021a). Therefore, the World Health Organization (WHO), the Africa Center for Disease Control (CDC), and the African Union Commission for Social Affairs issued statements welcoming the use of herbal preparations for COVID-19 management (WHO, 2020b).

Evidence from different findings suggested that herbal preparations can reduce the severity of the disease and prevent COVID-19 infection (Chan et al., 2020; Musoke et al., 2021b; Vellingiri et al., 2020). Traditional herbal Chinese preparations have shown appreciable results in improving clinical symptoms and reducing mortality and recurrence rates of the virus (Liang et al., 2021; Luo et al., 2020). Furthermore, China and India have used herbal preparations in combination with other conventional medicines to improve the immunity of patients (Ni et al., 2020; Shankar et al., 2020; Wang et al., 2020).

Nevertheless, different findings suggested that herbal preparations have an effective therapeutic component when combined with conventional medicine in COVID-19 management (Ang et al., 2020; Panyod et al., 2020). Using herbal preparations for therapeutic purposes should not be underestimated since many botanical drugs show antiviral efficacy. Furthermore, the review of several African scientific research (Okaiyeto & Oguntibeju, 2021) has shown that African plants have demonstrated antiviral activity. In West Africa, several herbal preparations were documented to be used during the Ebola Virus outbreak; however, none were studied in conventional clinical trials (Suk et al., 2016).

Moreover, Tanzania harbours 24% of the globally known biodiversity hotspots. It is endowed with about 31% of the African flora, of which about 9% have natural products of pharmacological and economic importance (United Republic of Tanzania, 2014). This puts the country in a better position to contribute to managing the COVID-19 conditions in the country and other countries worldwide. Further, herbal preparations are well prepared and utilized from the family to the commercial levels. The use of herbal preparations in Tanzania continues to be important in primary health care in the country. These herbal preparations include NIMRCAF, Covidol, Covotanxa, Bingwa, Planet++, Uzima and Bupiji essential oil. Most herbal preparations' common ingredients include ginger, garlic, lemongrass, eucalyptus, and clove. Initially, these herbal preparations were tested for the presence of any toxicity indications at the Government Chemist Laboratory Authority of Tanzania. They were revealed to be non-toxic for human use and hence merit an observational study in humans to ascertain their safety (GCLA, 2020). Thereafter, they were approved by the Traditional and Alternative Health Council of Tanzania for use among COVID-19 patients and other related conditions.

This study was, therefore, conducted to assess clinical outcomes (subsiding of the signs and symptoms related to COVID-19 as well as conversion of the RT-PCR results) and patient health outcomes (alive or dead) among COVID-19 patients receiving treatment at 12 health facilities in Tanzania Mainland.

Materials and methods

Study design and setting

This observational cohort study aimed to assess herbal preparations' safety and health outcomes among COVID-19 patients in Tanzania. This study was conducted between February and May 2021 at 12 (10 public and 2 private) health facilities, which were purposefully selected because they were among the health facilities with high COVID-19 patients. The public health facilities included Muhimbili National Hospital, Jakaya Kikwete Cardiac Institute, Bugando Medical Centre, Kilimanjaro Christian Medical Centre and Benjamini Mkapa Hospitals. Other public health facilities included Amana, Temeke, Mwananyamala and Dodoma Regional Referral Hospitals. The private facilities were Shree Hindu Mandal and Kairuki Hospitals.

Study population and cohorts/groups

We approached patients hospitalized with COVID-19 in the study sites. Eligible participants were those confirmed to have COVID-19 by RT-PCR, aged 18 years and above, who consented to be part of the study. Patients with a known history of liver disease or chronic kidney disease were excluded. The study participants were categorized into two groups: One group included those who received standard care alone, and the other comprised those who received standard care and were supplemented with herbal preparations.

Sample size calculation

Our assumptions regarding the expected change in proportions of COVID-19 patients using herbal preparations were that 25% of them would have improved symptoms or clinical signs compared to the cohort using standard treatment alone. Considering alpha of 5%, Power (1−β) of 80%, and using two proportions two-sided, non-inferiority comparison, we ended up with an estimated sample size of 62 patients per study group. The plan was to have eight groups of participants, of which seven would have been constituted by those using any of the approved herbal preparations plus standard care, and the remainder group included the participants who were on standard care alone. Overall, our target sample size was 500 study participants. However, due to the downslope of the COVID-19 second wave in the country, only 285 participants were enrolled.

Recruitment of the study participants

Medical personnel at the study sites attending to the COVID-19 patients were used to implement the study, including conducting interviews with the study participants. Since this was an observational study, healthcare providers only prescribed standard care treatment and were not involved in prescribing the herbal preparations. The participants determined their willingness to use or not use the herbal preparations. The research team focused on conducting interviews, observing, and recording health outcomes among the cohorts.

Participants were consecutively recruited, and we managed to enrol only 57% (n=285) of the required sample size because of the absence of more admitted COVID-19 patients as the pandemic was ending. Each Participant was followed up for 14 days. The participant was terminated from the study if they had completed 14 days of follow-up, withdrew from the study, were lost to follow-up after being discharged from the hospital or died within the follow-up period. If the participant still had COVID-19-related signs and symptoms or RT-PCR for Coronavirus was still positive, the participant was left to continue with the standard care management at the respective health facility.

Data collection

Face-to-face interviews were conducted with the eligible and consented study participants using a structured questionnaire. Interviews gathered information such as the history of using any of the

herbal preparations, name of the preparation used and duration of use, the experience of any adverse event (DAIDS Safety, 2010) on the due course of using the preparation (development of any new or worsening of the event). Participant's medical records were accessed to document sociodemographic information, clinical presentation on admission, past medical history, and baseline and follow-up laboratory records. Furthermore, mobile phone numbers were also collected for follow-up in case the participants were discharged before completing the follow-up duration. Data collection was done at baseline, day 7 and day 14. RT-PCR for Coronavirus was done at baseline for diagnosis and on days 7 and 14 for conversion assessment. Lactate dehydrogenase (LDH), D-dimer and ferritin levels were done for severity assessment at baseline and day 14.

Ethical consideration

The protocol for this study was approved by the National Health Research Ethics Subcommittee (NatHREC) in Tanzania, with ethical clearance number NIMR/HQ/R.8a/Vol. IX/3620. All study participants were 18 or older, and each provided written informed consent.

Data Analysis

The survey tool was programmed into and administered using Android tablets that contained an Open Data Kit (ODK). The programming process involved setting range and consistency checks to ensure the quality of the data collected was good. Field supervisors cleaned and synchronised the data on the NIMR main server in real-time. Data was exported from ODK to Excel in CSV format and later to Stata version 15 (STATA et al., USA) for further cleaning and analysis.

Results were presented as a comparison of the proportions of patients recovering from symptoms or clinical signs, proportions with RT-PCR conversion at day 7 or day 14 and the proportions of the health outcome (alive and dead) among COVID-19 patients in their respective cohorts. The probability and associated relative risks of all these endpoint events were compared on days 7 and 14 among COVID-19 patients in the cohorts. Pearson Chi-square statistics test was used to compare group differences for categorical variables. Bar graphs and tables were used to present the results pictorially. Outcome indicator rates and proportions were generated and compared mainly between herbal and non-herbal users. The prevalence of mortality in all COVID-19 patients, herbal users and non-herbal users was above 10%; thus, prevalence risk ratios (PRR) were estimated using the Modified Poison Logistic Regression Model, and we reported their 95% confidence interval (CI). This model was used since Classical Logistic Regression end up with wide confidence intervals once used to fit the model when the outcome of interest is greater than 10%; hence it is recommended when the outcome is less or equal to 10% (Fonseca Martinez et al., 2017; Thompson et al., 1998; Zou, 2004). We started with unadjusted models for each independent variable. All independent variables whose unadjusted prevalence risk ratio (RR) was significant at $p<0.20$ were candidates for multivariable analysis (Bursac et al., 2008; Gelman, 2013). Results were considered statistically significant if the p-value was <0.05.

Results

Socio-Demographic Characteristics of the Participants.

285 participants were enrolled between February and May 2021 at 12 health facilities. Table 1 reports on the sociodemographic characteristics of the study participants. The mean age was 59.2 ± 16.5 years. Males constituted 56% of the study participants. Nearly one-third (n=91) were aged 50 years and above. Seventy-two per cent (n=204) of the study participants reported having at least one form of co-morbidities, including diabetes, hypertension, asthma, Chronic Obstructive Pulmonary Diseases (COPD) and other forms of heart problems apart from hypertension. More than two-thirds (68.4%) reported using at least one form of herbal preparation.

Table 1: Socio-demographic characteristics of study participants at enrolment by herbal preparations use status (N=285).

Variable	Using Herbal preparation				Total	
	Yes		No			
	N	%	N	%	N	%
Age (years)						
Mean (SD)	58.0(15.9)		61.8(17.4)		59.2(16.5)	
Age group (in Years)						
<50	56	28.7	17	18.9	73	25.6
50 – 69	84	43.1	37	41.1	121	42.5
≥ 70	55	28.2	36	40.0	91	31.9
Sex						
Male	106	54.4	53	58.9	159	55.8
Female	89	45.6	37	41.1	126	44.2
Participants with at least one form of co-morbidities						
No	55	28.2	26	28.9	81	28.4
Yes	140	71.8	64	71.1	204	71.6
Region						
Dodoma	26	13.3	17	18.9	43	15.1
Mwanza	16	8.2	35	38.9	51	17.9
Kilimanjaro	43	22.1	11	12.2	54	19
Dar es salaam	110	56.4	27	30.0	137	48.1
Total	**195**	**100.0**	**90**	**100.0**	**285**	**100**

Type of herbal preparations reported to be used by the study participants

Here, we provide only information for those who have used the herbal preparations (n=195). During the interview, more than two-thirds (68.4%, n=195) of the 285 study participants reported using at least one form of herbal preparations. Figure 1 summarizes information on these different types of herbal preparations. Fifty-one per cent of these 195 participants (who were supplementing standard care with herbal preparations) reported using at least one of the seven herbal preparations used in this study. On the other hand, 49% of participants reported using homemade remedies containing mixtures of ginger, lemon, garlic, lemon grass, eucalyptus, and clove.

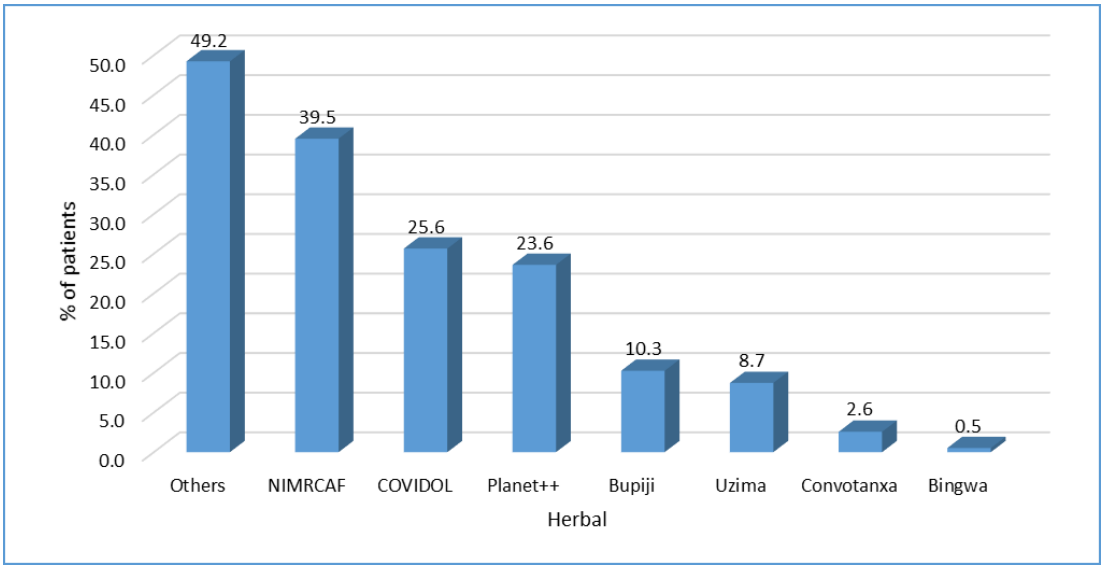

Figure 1: Type of herbal preparations reported to be used by the study participants (n=195)

Clinical symptoms and signs that study participants presented with at enrolment (N=285)

Figure 2 reports on the symptoms that study participants presented with at enrolment. The majority (88.8%) of participants presented with difficulty in breathing, followed by dry cough (78.6%) and fatigue (74.7%). The least reported symptoms were diarrhoea (9.8%) and runny nose (8.1%).

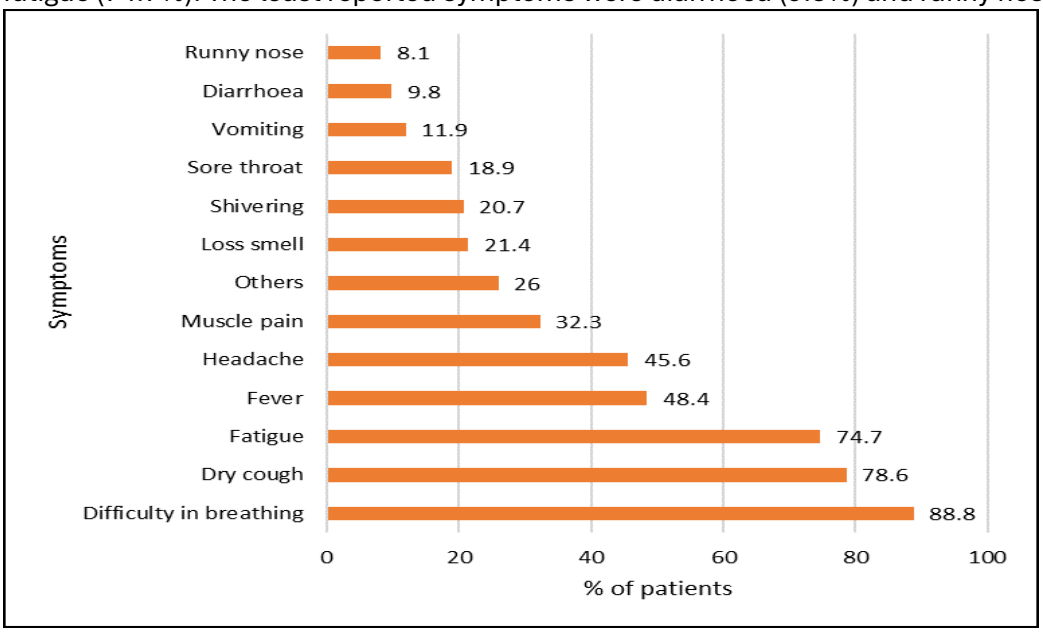

Figure 2: Type of symptoms that the study participants presented with at enrolment (N=285)

Duration of resolution of symptoms among herbal and non-herbal users (N=285)

During enrollment, difficulty in breathing (88.2% vs 90%), dry cough (79% vs 77.8%), fatigue (77.4% vs 68.9%), fever (46.7% vs 52.2%) and headache (46.2% vs 44.4%) were mostly reported by herbal and non-herbal users respectively (Table 2). By day 7, the proportion of study participants who reported still having trouble breathing was 48.7% and 40.7 %; dry cough (46.6% vs 48.6%); fatigue (48% vs 53.7%); fever (8.8% vs 11.1%) and headache (9.5% vs 20.4%) among users and non-herbal users respectively. On day 14, nearly all participants had resolved symptoms, and few were still

presenting with difficulty in breathing (23.3%), dry cough (22.3% vs 36.7%), fatigue (38.9% vs 50%); fever (4.9% vs 1.1%) and headache (6.8% vs 10.0%) among users and non- herbal users respectively.

Table 2: Symptoms among the herbal and non-herbal users at day 0, 7 and 14

Symptoms	Using herbal preparations: Day 0 n=285 Yes, n=195(%)	No, n=90(%)	Using herbal preparations: Day 7 n=202 Yes n=148(%)	No n=54(%)	Using herbal preparations: Day 14 n=133 Yes n=103(%)	No n=30
Fever	91(46.7)	47(52.2)	13(8.8)	6(11.1)	5(4.9)	1(1.1)
Shivering	34(17.4)	25(27.8)	4(2.7)	1(1.9)	1(1.0)	0(0.0)
Dry cough	154(79.0)	70(77.8)	69(46.6)	26(48.6)	23(22.3)	11(36.7)
Vomiting	19(9.7)	15(16.7)	1(0.7)	1(1.9)	1(1.0)	1(3.33)
Diarrhea	20(10.2)	8(8.9)	6(4.1)	0(0.0)	1(1.0)	0(0.0)
Headache	90(46.2)	40(44.4)	14(9.5) *	11(20.4)	7(6.8)	3(10.0)
Difficulty in breathing	172(88.2)	81(90.0)	72(48.7)	22(40.7)	24(23.3)	7(23.3)
Runny nose	13(6.7)	10(11.1)	0(0.0)	0(0)	1(0.97)	0(0.0)
Sore throat	35(18.0)	19(21.1)	17(11.5)	4(7.4)	4(3.9)	0(0.0)
Fatigue	151(77.4)	62(68.9)	71(48)	29(53.7)	40(38.9)	15(50)
Muscle pain	60(30.8)	32(35.6)	19(12.8)	8(14.8)	8(7.8)	2(6.67)
Loss smell	41(21.0)	20(22.2)	6(4.1)	4(7.4)	1(1.0)	0(0.0)

Findings from the Physical and Clinical assessments among study participants at baseline, day 7 and day 14

Vital signs and physical examinations were done at baseline, days 7 and 14, for all study participants. During enrolment, more than 50% of the study participants presented with low oxygen saturation (<92% SPO_2) (Table 3). There was no significant difference between the two groups. The majority (about 80%) had normal physical findings except the respiratory system, where more than three-quarters (78.1%) of the herbal users had abnormal findings compared to 56.7% of non-herbal users. On the 7th day of follow-up, 38.5% of herbal users still had abnormal oxygen saturation compared to 44.4% of non-herbal users. The respiratory system was abnormal in 48.7% and 35.2% of herbal users and non-users, respectively. Furthermore, on day 14, less than 1/3 (<33%) of the participants, both herbal and non-herbal users, had abnormal oxygen saturation and respiratory physical findings.

Table 3: Physical and Clinical assessment among herbal users and non-users at baseline (N=285)

Variable	Herbal users n=195 (%)		Non-Herbal users n=90 (%)	
	Normal	Abnormal	Normal	Abnormal
Vital Signs				
Temperature	162(82.6)	34(17.4)	72(80.0)	18(20.0)
Oxygen Saturation	72(36.7)	124(63.3)	34(37.8)	56(62.2)
Respiratory rate	87(44.4)	109(55.6)	38(42.2)	52(57.8)
Heart rate	125(63.8)	71(36.2)	53(58.9)	37(41.1)
Systolic blood pressure	131(66.8)	65(33.2)	60(66.7)	30(33.3)
Diastolic blood pressure	145(74.0)	51(26.0)	67(74.4)	23(25.6)

RBG	142(79.8)	36(20.2)	62(78.5)	17(21.5)
Physical Examination				
General Appearance				
Respiratory	43(21.9)	153(78.1)***	39(43.3)	51(56.7)
Cardiovascular	164(83.7)	32(16.3)	75(83.3)	15(16.7)
Abdominal/ Gastrointestinal	172(87.8)	24(12.2)	83(92.2)	7(7.8)
Urogenital	178(96.7)	6(3.3)	86(93.0)	6(7.0)
Musculoskeletal	171(87.2)	25(12.8)	72(80.0)	18(20.0)
Neurological	187(95.4)	9(4.6)	81(90.0)	9910.0)
Psychological	166(85.6)	28(14.4)	70(77.8)	20(22.2)
Haematological/ Lymphatic	184(93.9)	12(6.1)	83(92.2)	7(7.8)
Skin/ Dermatological	191(97.4)	5(2.6)	89(98.9)	1(1.1)

Duration of RT-PCR status of the study participants to convert to RT-PCR Negative

All study participants were RT-PCR positive during enrolment. On day 7, RT-PCR information was available for 184 (146 herbal users and 38 non-users) participants. Nearly two-thirds (n=120) had converted to RT-PCR negative. Conversion was higher among non-herbal users than herbal users (78% vs. 61%).

On the other hand, on day 14, RT-PCR information was available for 67 (56 herbal users and 11 non-herbal users) study participants. Overall, 60% of these participants had negative PCR results. Among the participants with negative PCR results, 64.3% were herbal users compared to 36.4% non-herbal users (Figure 3).

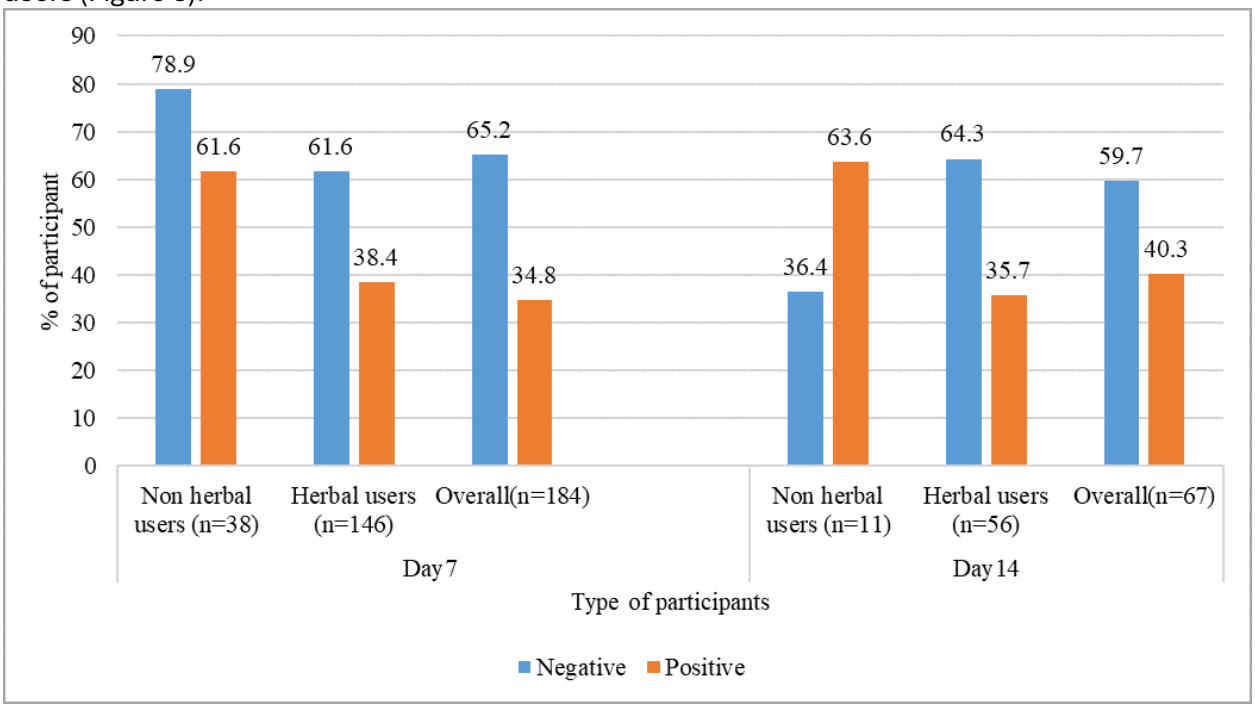

Figure 3: RT-PCR conversion at day 7 and 14 (n=67)

Health outcomes among study participants (N=285)

Of 285 enrolled participants, 54 (18.8%) died during the study period. Overall, proportionally mortality was higher among those who used standard care alone (non-herbal users) (n=21, 23.3%) compared to among those who supplemented standard care with herbal preparations (herbal users) (n=33, 16.9%), as shown in Figure 4. Further, an assessment of factors associated with mortality among COVID-19 patients using herbals and non-herbal users was done using Modified Poison Regression analysis involving adjustment for age and sex. Of these, only COVID-19 severity status was significantly associated with mortality, more among non-herbal users (APR=3.4, at 95%CI 1.5-8.1 with) compared to among herbal users (APR=2.3, at 95%CI 1.2-4.5). Other factors such as age, comorbidities, body mass index and inflammatory markers (d-Dimer, Ferritin and LDH) were not associated with mortality among COVID-19 patients in both groups.

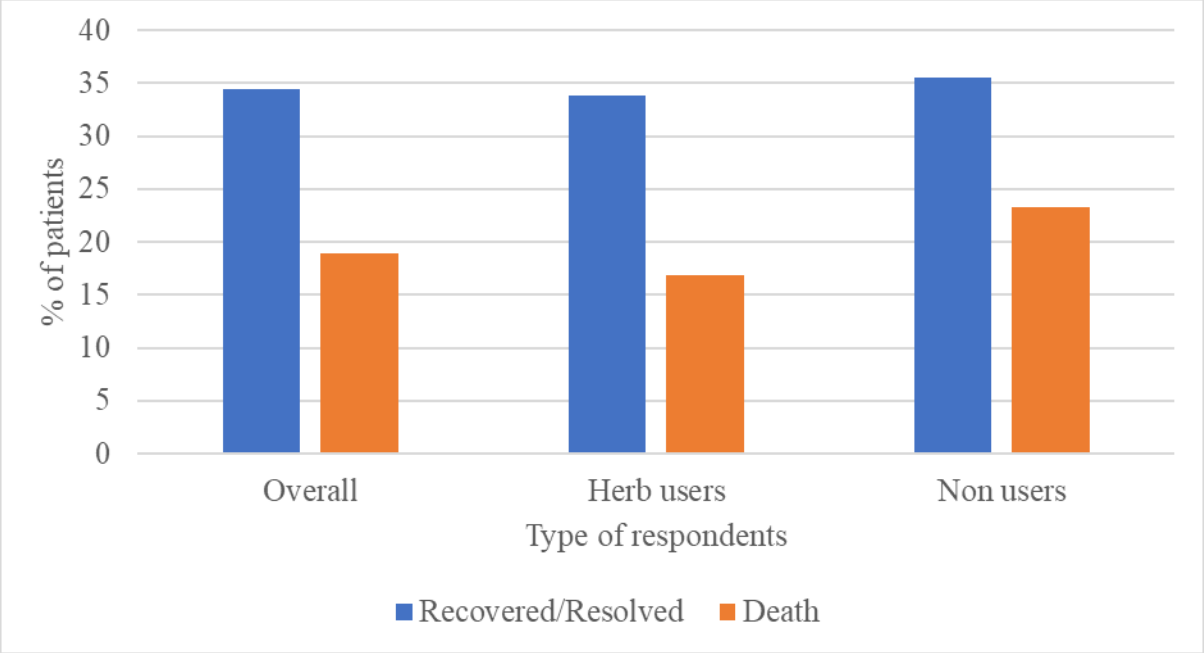

Figure 4: Patients' outcomes by herbal use status

Discussion

This study aimed to assess clinical presentations and outcomes among COVID-19 patients receiving standard care alone compared to those receiving standard care supplemented with herbal preparations. The findings reported that nearly three-quarters of the participants were 50 years and above, which is one of the risk factors for poor health outcomes among COVID-19 patients (Kaso et al., 2022; Li et al., 2021). Literature shows that comorbidities are the risk factor for severe COVID-19 and mortality (Booth et al., 2021a; Geng et al., 2021a). This study has also shown that 71% and 72% of the herbal users and non-herbal users had at least one form of co-morbidities, respectively, that posed a risk of poor health outcomes.

The findings showed that more than two-thirds (68.4%) of the participants reported using at least one form of herbal preparations. Herbal medicinal product use has increased tremendously over the past decades, and people worldwide rely on them in different healthcare settings (WHO, 2004, 2013). Moreover, in the COVID-19 era, there was increased use of herbal preparations with medicinal effects that had the capacity to modulate the immune response; hence, they were believed to have beneficial effects on preventing or treating COVID-19 (Kocaadam & Şanlier, 2017; Sharma et al., 2009).

Most symptoms (dry cough, fever, headache, and difficulty breathing) reported by participants during enrolment had resolved by day 7 more among study participants who were on herbal preparations than their counter group. By day 14, nearly all symptoms had resolved in both the participants using and not using herbal preparations. Similarly, in other studies, the median interval for symptom resolution ranged from 4 to 11 days from the enrollment date (Lubart et al., 2021; Tenforde et al., 2020). Furthermore, studies conducted in China showed significant improvement in symptoms among participants using herbal preparations for COVID-19 treatment compared to the group under standard care treatment (Ang et al., 2020; SUN et al., 2020).

Additionally, the findings from this study revealed that more than two-thirds of the participants had PCR conversion by day 7, and conversion was higher among non-herbal users than their counterparts. On the other hand, on day 14, the PCR conversion to negative was higher among the herbal users than their counterparts. The duration of PCR conversion observed in this study appeared to be longer than reported elsewhere (Deng et al., 2020; Zheng et al., 2020).

Furthermore, this study observed the use of herbal preparations and their effect on mortality among COVID-19 patients. In this study, we observed an overall mortality of 18.8%, and mortality was proportionally higher among non-herbal users compared to herbal users (55% to 60%). Other studies have reported similar findings (Oliveira et al., 2021).

Our study reported that proportionally, more non-herbal users progressed to a severe form of COVID-19 compared to their counterparts, and it was associated with a higher rate of mortality among non-herbal users. Other factors such as age, comorbidities, inflammatory markers, and body mass index were not associated with mortality. On the other hand, advanced age is reported elsewhere as one of the risk factors for severe forms of COVID-19 as well as COVID-19-related mortality (Alwafi et al., 2021; Booth et al., 2021b; Ciceri et al., 2020; Geng et al., 2021b).

Study Limitation

The design of the current study is subject to limitations. Due to the study's prospective nature, attaining the desired sample size was impossible because of the downsloping of the COVID-19 wave, which affected the recruitment of participants in most of the study sites. Moreover, healthcare providers were not involved in prescribing the herbal preparations as the use of herbal preparations was upon the participant's decision. Hence, this led to limited participants in some cohorts due to the facilities' uneven distribution of herbal preparations. However, this study is among the first to investigate clinical outcomes and patient health outcomes among COVID-19 patients supplemented with approved herbal preparations in this population. Therefore, it could become a basis for other studies with a larger population nationwide.

Conclusion

This study revealed that the use of herbal preparations in addition to standard care treatment has positive effects on the subsidence of the duration of presenting symptoms and signs and a reduction in the proportion of mortality among COVID-19 patients. However, further research, especially clinical trials, may be needed to ascertain these findings.

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Authors' contributions: GDK, VKB, DCB, LLS, EPM, CAM, FPM, JNT, MSK, SPE, LSM, ES, MH, RSN, PKP, LV and JJO designed the study. GBK and GDK analyzed the data. GDK, VKB, DCB, LLS, JNT, SPE, CAM, FPM drafted the manuscript. GDK, VKB, DCB, LLS, JNT, SPE, CAM, FPM, ANM, and PPM reviewed manuscript drafts. The author(s) read and approved the final manuscript.

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Conflicts of interest: The authors declare no competing interests.

Data availability: The main text reports all important data and methods. The corresponding author makes additional datasets used and/or analyzed during the current study available upon reasonable request.

Reference

Agyei-Baffour, P., Kudolo, A., Quansah, D. Y., & Boateng, D. (2017). Integrating herbal medicine into mainstream healthcare in Ghana: Clients' acceptability, perceptions and disclosure of use. *BMC Complementary and Alternative Medicine*, *17*(1), 1–9. https://doi.org/10.1186/s12906-017-2025-4

Alwafi, H., Naser, A. Y., Qanash, S., Brinji, A. S., Ghazawi, M. A., Alotaibi, B., Alghamdi, A., Alrhmani, A., Fatehaldin, R., Alelyani, A., Basfar, A., Albarakati, A., Alsharif, G. F., Obaid, E. F., & Shabrawishi, M. (2021). Predictors of length of hospital stay, mortality, and outcomes among hospitalised COVID-19 patients in Saudi Arabia: A cross-sectional study. *Journal of Multidisciplinary Healthcare*, *14*, 839–852. https://doi.org/10.2147/JMDH.S304788

Ang, L., Song, E., Lee, H. W., & Lee, M. S. (2020). Herbal medicine for the treatment of coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis of randomized controlled trials. *Journal of Clinical Medicine*, *9*(5), 1–20. https://doi.org/10.3390/jcm9051583

Attah, A. F., Fagbemi, A. A., Olubiyi, O., Dada-Adegbola, H., Oluwadotun, A., Elujoba, A., & Babalola, C. P. (2021). Therapeutic Potentials of Antiviral Plants Used in Traditional African Medicine With COVID-19 in Focus: A Nigerian Perspective. *Frontiers in Pharmacology*, *12*(April), 1–38. https://doi.org/10.3389/fphar.2021.596855

Booth, A., Reed, A. B., Ponzo, S., Yassaee, A., Aral, M., Plans, D., Labrique, A., & Mohan, D. (2021a). Population risk factors for severe disease and mortality in COVID-19: A global systematic review and meta-analysis. *PLoS ONE*, *16*(3 March), 1–30. https://doi.org/10.1371/journal.pone.0247461

Booth, A., Reed, A. B., Ponzo, S., Yassaee, A., Aral, M., Plans, D., Labrique, A., & Mohan, D. (2021b). Population risk factors for severe disease and mortality in COVID-19: A global systematic review and meta-analysis. *PLoS ONE*, *16*(3 March), 1–30. https://doi.org/10.1371/journal.pone.0247461

Bursac, Z., Gauss, C. H., Williams, D. K., & Hosmer, D. W. (2008). Purposeful selection of variables in logistic regression. *Source Code for Biology and Medicine*, *3*, 1–8. https://doi.org/10.1186/1751-0473-3-17

Chan, K. W., Wong, V. T., & Tang, S. C. W. (2020). COVID-19: An Update on the Epidemiological, Clinical, Preventive and Therapeutic Evidence and Guidelines of Integrative Chinese-Western Medicine for the Management of 2019 Novel Coronavirus Disease. *American Journal of Chinese Medicine*, *48*(3), 737–762. https://doi.org/10.1142/S0192415X20500378

Ciceri, F., Castagna, A., Rovere-Querini, P., De Cobelli, F., Ruggeri, A., Galli, L., Conte, C., De Lorenzo, R., Poli, A., Ambrosio, A., Signorelli, C., Bossi, E., Fazio, M., Tresoldi, C., Colombo, S., Monti, G., Fominskiy, E., Franchini, S., Spessot, M., … Zangrillo, A. (2020). Early predictors of clinical outcomes of COVID-19 outbreak in Milan, Italy. *Clinical Immunology*, *217*, 108509. https://doi.org/10.1016/j.clim.2020.108509

DAIDS Safety. (2010). *Manual for Expedited Reporting of Adverse Events to DAIDS*. *January*, 1–16.

Deng, W., Guang, T. W., Yang, M., Li, J. R., Jiang, D. P., Li, C. Y., & Wang, D. X. (2020). Positive results for patients with COVID-19 discharged form hospital in Chongqing, China. *BMC Infectious Diseases*, *20*(1), 1–6. https://doi.org/10.1186/s12879-020-05151-y

Fonseca Martinez, B. A., Leotti, V. B., Silva, G. de S. e., Nunes, L. N., Machado, G., & Corbellini, L. G. (2017). Odds ratio or prevalence ratio? An overview of reported statistical methods and appropriateness of interpretations in cross-sectional studies with dichotomous outcomes in veterinary medicine. *Frontiers in Veterinary Science*, *4*(NOV), 1–8. https://doi.org/10.3389/fvets.2017.00193

GCLA. (2020). Government Chemist Laboratory Authority (GCLA) : Home. In *GCLA Website*.

Gelman, A. (2013). P values and statistical practice. *Epidemiology*, *24*(1), 69–72. https://doi.org/10.1097/EDE.0b013e31827886f7

Geng, M. J., Wang, L. P., Ren, X., Yu, J. X., Chang, Z. R., Zheng, C. J., An, Z. J., Li, Y., Yang, X. K., Zhao, H. T., Li, Z. J., He, G. X., & Feng, Z. J. (2021a). Risk factors for developing severe COVID-19 in China: an analysis of disease surveillance data. *Infectious Diseases of Poverty*, *10*(1), 1–10. https://doi.org/10.1186/s40249-021-00820-9

Geng, M. J., Wang, L. P., Ren, X., Yu, J. X., Chang, Z. R., Zheng, C. J., An, Z. J., Li, Y., Yang, X. K., Zhao, H. T., Li, Z. J., He, G. X., & Feng, Z. J. (2021b). Risk factors for developing severe COVID-19 in China: an analysis of disease surveillance data. *Infectious Diseases of Poverty*, *10*(1), 1–10. https://doi.org/10.1186/s40249-021-00820-9

Kaso, A. W., Hareru, H. E., Kaso, T., & Agero, G. (2022). Factors Associated with Poor Treatment Outcome among Hospitalized COVID-19 Patients in South Central, Ethiopia. *BioMed Research International*, *2022*. https://doi.org/10.1155/2022/4551132

Kocaadam, B., & Şanlier, N. (2017). Curcumin, an active component of turmeric (Curcuma longa), and its effects on health. *Critical Reviews in Food Science and Nutrition*, *57*(13), 2889–2895. https://doi.org/10.1080/10408398.2015.1077195

Li, Y., Ashcroft, T., Chung, A., Dighero, I., Dozier, M., Horne, M., McSwiggan, E., Shamsuddin, A., & Nair, H. (2021). Risk factors for poor outcomes in hospitalised COVID-19 patients: A systematic review and meta-analysis. *Journal of Global Health*, *11*, 1–11. https://doi.org/10.7189/jogh.11.10001

Liang, S. B., Zhang, Y. Y., Shen, C., Liang, C. H., Lai, B. Y., Dai, N., Li, Y. Q., Tian, Z. Y., Zhang, X. W., Jiang, Y., Xiong, M., Zhang, Y. P., Zhang, Y., Robinson, N., & Liu, J. P. (2021). Chinese Herbal Medicine Used With or Without Conventional Western Therapy for COVID-19: An Evidence Review of Clinical Studies. *Frontiers in Pharmacology*, *11*(February). https://doi.org/10.3389/fphar.2020.583450

Lubart, E., Gal, G., Mizrahi, E. H., Tzabary, A., Baumohl, E., Pinco, E., Idkiedek, Z., Ali, E. H., Berger, M., & Goltsman, G. (2021). Time to resolution of infection in COVID-19 patients:

the experience of a tertiary medical center in Israel. *Japanese Journal of Infectious Diseases*, JJID-2021.

Luo, L., Jiang, J., Wang, C., Fitzgerald, M., Hu, W., Zhou, Y., Zhang, H., & Chen, S. (2020). Analysis on herbal medicines utilized for treatment of COVID-19. *Acta Pharmaceutica Sinica B*, *10*(7), 1192–1204. https://doi.org/10.1016/j.apsb.2020.05.007

Musoke, P., Masajjage, J., Kisuule, I., Nantaayi, B., Ssewante, N., & Bongomin, F. (2021a). *A Preliminary Report on Herbal Medicine Use Among Patients Hospitalized at Two-Large COVID-19 Treatment Centers in Uganda*. 4609–4617.

Musoke, P., Masajjage, J., Kisuule, I., Nantaayi, B., Ssewante, N., & Bongomin, F. (2021b). *A Preliminary Report on Herbal Medicine Use Among Patients Hospitalized at Two-Large COVID-19 Treatment Centers in Uganda*. 4609–4617.

Ni, L., Zhou, L., Zhou, M., Zhao, J., & Wang, D. W. (2020). Combination of western medicine and Chinese traditional patent medicine in treating a family case of COVID-19. *Frontiers of Medicine*, *14*(2), 210–214. https://doi.org/10.1007/s11684-020-0757-x

Okaiyeto, K., & Oguntibeju, O. O. (2021). African herbal medicines: Adverse effects and cytotoxic potentials with different therapeutic applications. In *International Journal of Environmental Research and Public Health* (Vol. 18, Issue 11). MDPI AG. https://doi.org/10.3390/ijerph18115988

Oliveira, E., Parikh, A., Lopez-Ruiz, A., Carrilo, M., Goldberg, J., Cearras, M., Fernainy, K., Andersen, S., Mercado, L., Guan, J., Zafar, H., Louzon, P., Carr, A., Baloch, N., Pratley, R., Silverstry, S., Hsu, V., Sniffen, J., Herrera, V., & Finkler, N. (2021). ICU outcomes and survival in patients with severe COVID-19 in the largest health care system in central Florida. *PLoS ONE*, *16*(3 March), 1–14. https://doi.org/10.1371/journal.pone.0249038

Panyod, S., Ho, C. T., & Sheen, L. Y. (2020). Dietary therapy and herbal medicine for COVID-19 prevention: A review and perspective. *Journal of Traditional and Complementary Medicine*, *10*(4), 420–427. https://doi.org/10.1016/j.jtcme.2020.05.004

Shankar, A., Dubey, A., Saini, D., & Prasad, C. P. (2020). Role of Complementary and Alternative Medicine in Prevention and Treatment of COVID-19: An Overhyped Hope. *Chinese Journal of Integrative Medicine*, *26*(8), 565–567. https://doi.org/10.1007/s11655-020-2851-y

Sharma, M., Anderson, S. A., Schoop, R., & Hudson, J. B. (2009). Induction of multiple pro-inflammatory cytokines by respiratory viruses and reversal by standardized Echinacea, a potent antiviral herbal extract. *Antiviral Research*, *83*(2), 165–170. https://doi.org/10.1016/j.antiviral.2009.04.009

Suk, J. E., Jimenez, A. P., Kourouma, M., Derrough, T., Baldé, M., Honomou, P., Kolie, N., Mamadi, O., Tamba, K., Lamah, K., Loua, A., Mollet, T., Lamah, M., Nana Camara, A., & Prikazsky, V. (2016). Post-ebola measles outbreak in lola, Guinea, January-June 2015. *Emerging Infectious Diseases*, *22*(6), 1106–1108. https://doi.org/10.3201/eid2206.151652

SUN, H., Xu, F., ZHANG, L., WEI, C., CHEN, J., WANG, Q., & JIA, Z. (2020). Study on clinical efficacy of Lianhua Qingke granule in treatment of mild and ordinary COVID-19. *Chinese Journal of Experimental Traditional Medical Formulae*, 29–34.

Tenforde, M. W., Kim, S. S., Lindsell, C. J., Billig Rose, E., Shapiro, N. I., Files, D. C., Gibbs, K. W., Erickson, H. L., Steingrub, J. S., Smithline, H. A., Gong, M. N., Aboodi, M. S., Exline, M. C., Henning, D. J., Wilson, J. G., Khan, A., Qadir, N., Brown, S. M., Peltan, I. D., … Wu, M. J. (2020). Symptom Duration and Risk Factors for Delayed Return to Usual Health Among[1] M. W. Tenforde et al., "Symptom Duration and Risk Factors for Delayed Return

to Usual Health Among Outpatients with COVID-19 in a Multistate Health Care Systems Network — United. *MMWR. Morbidity and Mortality Weekly Report*, *69*(30), 993–998.

Thompson, M. Lou, Myers, J. E., & Kriebel, D. (1998). Prevalence odds ratio or prevalence ratio in the analysis of cross sectional data: What is to be done? *Occupational and Environmental Medicine*, *55*(4), 272–277. https://doi.org/10.1136/oem.55.4.272

United Republic of Tanzania. (2014). Fifth National Report on the Implementation of the Convention on Biological Diversity. In *I* (Issue 1).

Vellingiri, B., Jayaramayya, K., Iyer, M., & Narayanasamy, A. (2020). *Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information . January*.

Wang, J. bo, Wang, Z. xia, Jing, J., Zhao, P., Dong, J. hui, Zhou, Y. feng, Yang, G., Niu, M., Zhao, X., Jiang, T. jun, Bi, J. feng, Xu, Z., Zhang, P., Wu, D., Bai, Z. fang, Guo, Y. ming, Yu, S. miao, Sun, Y. qiang, Zhang, Z. teng, … Xiao, X. he. (2020). Exploring an Integrative Therapy for Treating COVID-19: A Random1. Wang J bo, Wang Z xia, Jing J, Zhao P, Dong J hui, Zhou Y feng, et al. Exploring an Integrative Therapy for Treating COVID-19: A Randomized Controlled Trial. Chin J Integr Med. 2020;26(9): *Chinese Journal of Integrative Medicine*, *26*(9), 648–655.

WHO. (2004). *WHO Guidelines on Safety Monitoring of Herbal Medicines in Pharmacovigilance Systems.[Google Scholar]*.

WHO. (2013). *WHO traditional medicine strategy. 2014-2023*. World Health Organization.

WHO. (2020a). *Expert panel endorses protocol for COVID-19 herbal medicine clinical trials*.

WHO. (2020b). *Expert panel endorses protocol for COVID-19 herbal medicine clinical trials*. https://www.afro.who.int/pt/node/13374

Zheng, S., Fan, J., Yu, F., Feng, B., Lou, B., Zou, Q., Xie, G., Lin, S., Wang, R., Yang, X., Chen, W., Wang, Q., Zhang, D., Liu, Y., Gong, R., Ma, Z., Lu, S., Xiao, Y., Gu, Y., … Liang, T. (2020). Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: Retrospective cohort study. *The BMJ*, *369*(March), 1–8. https://doi.org/10.1136/bmj.m1443

Zou, G. (2004). A Modified Poisson Regression Approach to Prospective Studies with Binary Data. *American Journal of Epidemiology*, *159*(7), 702–706. https://doi.org/10.1093/aje/kwh090