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Biopsychosocial analysis of antibiotic use for the prevention or management of COVID-19 infections: A scoping review

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ABSTRACT

Background: The novelty and complexity of the COVID-19 pandemic has resulted in various coping mechanisms adopted by individuals as a means of averting the perceived fatalities of the pandemic. The use of antibiotics in the management of COVID-19 is clinically recommended under specific conditions. However, there are increasing trends of non-adherence to the recommended criteria resulting in the unwarranted use of antibiotics as an adaptative approach to the ongoing pandemic.
Objective: The objective was to identify and classify factors associated with the unwarranted use of antibiotics in the management of COVID-19 from published literature and the perspectives of key stakeholders along a Biopsychosocial model.
Methods: Literature was searched in the following databases: PubMed/MEDLINE, Scopus, Embase and Google Scholar for studies published between 31st December 2019 and 31st January 2022. The Arskey and O'Malley framework modified by Levac in the six-stage methodological process was adopted for this review and included: a) identification of research questions, b) identification of relevant research articles, c) selection of studies, d) data charting and synthesis, e) summary, discussion and analysis, and f) stakeholder consultations.
Results: Out of 10,252 records identified from all sources, 12 studies were selected for inclusion in this scoping review. The selected articles reflected both antibiotic use and COVID-19 whilst capturing the biological (medical) and psychosocial perspectives. Most of the studies reported the overuse or abuse of Azithromycin especially in hospital settings. Common themes across the review and stakeholder consultations included fear, anxiety, media influences and deficits in public knowledge.
Conclusion: The findings of the study highlight the complexity of antibiotic control especially in the context of a pandemic. The identified determinants of antibiotic use provide the necessary framework to simulate health emergencies and be better positioned in the future through the development of targeted and comprehensive policies on antibiotic stewardship.

1. Background

COVID-19 is a viral infectious disease caused by the coronavirus which manifests as a mild, moderate to severe respiratory illness in victims.[1] Similar to the profile of most viruses, the coronavirus is constantly mutating and resulting in genetic variation which may be potentially more virulent.[2] The COVID-19 syndrome is caused by a novel SARS-CoV-2 with self-limiting clinical manifestations mostly mild in children.[3]

As a typical viral disease, antibiotics are not the primary anti-infective agents adopted in the clinical management of COVID-19. However, the use of antibiotics in the clinical management of COVID-19 is not out of place since atypical antibiotics may improve the prognosis of viral infections through indirect immunomodulatory and anti-inflammatory mechanisms.[4,5] The virus can also predispose a patient to secondary bacterial infections which may require the general use of antibiotics.[6,7] The antibiotics become necessary due to the history of bacterial co-infections heightening the gravity of respiratory viral infections and subsequently causing death. However, some antibiotics have been found to possess antiviral effects exhibited by their ability to

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modulate the immune response and decrease inflammatory cytokines.[8–10] These effects have generated significant interest in their potential utilization in the treatment of COVID-19 infections.[11]

Bacterial co-infections occur in less than 4% of patients hospitalized with COVID-19. More so, the relationship between COVID-19 and bacterial secondary infections is still a grey area.[7,12] Notwithstanding, most patients with COVID-19 infection receive antibiotics regardless of the rarity of bacterial co-infections.[13] Common amongst the frequently used antibiotics for COVID-19 infections are fluoroquinolones, macrolides and cephalosporins.[14]

Even though antibiotics are mostly not needed in the treatment or prevention of COVID-19, a behavioral insights research in nine countries within the European region validates the increased use of antibiotic with increase in COVID-19 infection cases. The study goes on to report that 79%–96% of the antibiotic consumers are not infected with COVID-19 but were taking it as prophylaxis under the misconception that it could save them from COVID-19 [15]

The novelty and perceived fatalities of the coronavirus infection in the wake of the pandemic, has significantly advanced the unwarranted use of antibiotics.[15] A cause for concern as the misuse and overuse of antimicrobials is a significant factor found to be accelerating the life-threatening process of antimicrobial resistance.[16] The World Health Organization (WHO) describes antimicrobial resistance (AMR) as the "ability of a microorganism (bacteria, viruses, parasites etc) to stop an antimicrobial (antibiotics, antivirals and antimalarials) from working against it".[17] The culminating effect of AMR advanced by the unwarranted use of antibiotics is that conventional treatments are no longer effective. Thus, unresolved infections may result in death or may easily spread to others.[18] The unwarranted use of antibiotics in this context can be described as the inappropriate use of antibiotics through the overuse, unlicensed use, overprescribing and non-prescription use of antibiotics.

Emerging scientific literature on COVID-19 suggested various factors as key drivers of the unwarranted use of antibiotics in managing COVID-19 infection. These factors include medical overuse in hospital settings,[19] psychological distress causing fear and social reasons such as the limited knowledge about antibiotics.[20] Generally, the prevalence of the unwarranted use of antibiotics and its corresponding drivers and barriers have been well established in literature.[21,22,23] However, there have been limited reviews identifying the predisposing factors precipitating this trend of antibiotic misuse for the management of COVID-19 within the context of the pandemic[613]. This study sought to identify and classify the factors associated with the use of antibiotics in the management of COVID-19 from published literature and the perspectives of key stakeholders within the framework of the Biopsychosocial model. The Biopsychosocial model which was primarily conceptualized by George Engel posits that comprehending an individual's medical situation does not rest solely on the biological factors but also on the psychological and social factors.[24] The model is commonly used in addressing disease states and improving clinical outcomes by sensitizing clinicians of to the interaction among the biological, psychological, sociocultural, and spiritual factors in the management of diseases.[25]

2. Methods

2.1. Study design

A scoping review was conducted between November 2021 and January 2022 following the methodological framework proposed by Arskey and O'Malley[26] and advanced by Levac et al.[27] The six-stage methodological process included: a) identification of research questions, b) identification of relevant research articles, c) selection of studies, d) data charting and synthesis, e) summary, discussion and analysis, and f) stakeholder consultations.

The data was collated following the systematic collection and analysis of literature using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR).[28] The study was approved by the Ghana Health Service Ethics Committee on 11th October 2021 (GHS-ERC: 008/05/21) and the review protocol was registered in Open Science Framework[29]

2.1.1. Identification of research questions

The scoping review focused on investigating the inappropriate use of antibiotics in the management of COVID-19 from published literature and stakeholder perspectives. This was guided by the following research questions: (i) What are the types of antibiotics frequently used for COVID-19 prevention and treatment? (ii) What is the geographical distribution of unwarranted antibiotic use for COVID-19? (iii) What are the associated factors facilitating the unwarranted use of antibiotics in managing COVID-19 based on the bio-psychosocial framework?

2.1.2. Identification of relevant research articles

Literature for this review were identified and assessed by searching the following relevant databases: PubMed/MEDLINE, Scopus, Embase and Google Scholar. Scientific papers published after 31st December 2019 which was the date the World Health Organization (WHO) received its first communication on COVID-19[30] up until January 2022 were searched. The strategy adopted the use of the following Medical Subject Headings (MeSH) to search for articles in PubMed.

- COVID-19: This included the various terms for describing COVID-19; coronavirus, SARS-CoV-2, covid, pandemic
- Unwarranted: This included terms/synonyms for: unwarranted, misuse, overuse, abuse, self-medication, self-treatment, non-prescription
- Antibiotics: This included terms/synonyms for: antibiotics, antimicrobial, antibacterial, dispensing, medication, treatment
- Antibiotic Resistance: This included the terms used to describe antibiotic resistance; antimicrobial resistance, AMR, resistance, antibiotic failure
- Factors: This will include terms/synonyms for: factors, facilitators, barriers, drivers, and determinants.

These terms also formed part of the appropriate keywords adopted to search for articles in Google Scholar, Scopus and EMBASE.

Boolean operators were employed in the combination of the various key search terms to ensure that the selected articles reflected both antibiotic use and COVID-19 whilst capturing both biological (medical) and psychosocial perspectives.

2.2. Inclusion and exclusion criteria

For this review, unwarranted use of antibiotics which is the inappropriate use of antibiotics[31,32] was recognized as the misuse, overuse, unlicensed use, overprescribing and non-prescription use of antibiotics. The pre-set criteria for the selection of articles comprised:

2.2.1. Inclusion criteria

- Empirical studies: randomised controlled trials (RCTs), quasi-experimental studies, cross-sectional, case-control or cohort studies.

2.2.2. Exclusion criteria

- Opinion pieces, theoretical publications, and review articles
- Studies that were unavailable in English

2.3. Selection of studies

Two members of the research team (RAN and IAK) independently assessed the eligibility status of the various study papers. The assessment was done procedurally by a title and abstract screening followed by a full text screening (Fig. 1). Discrepancies on the eligibility of an article for

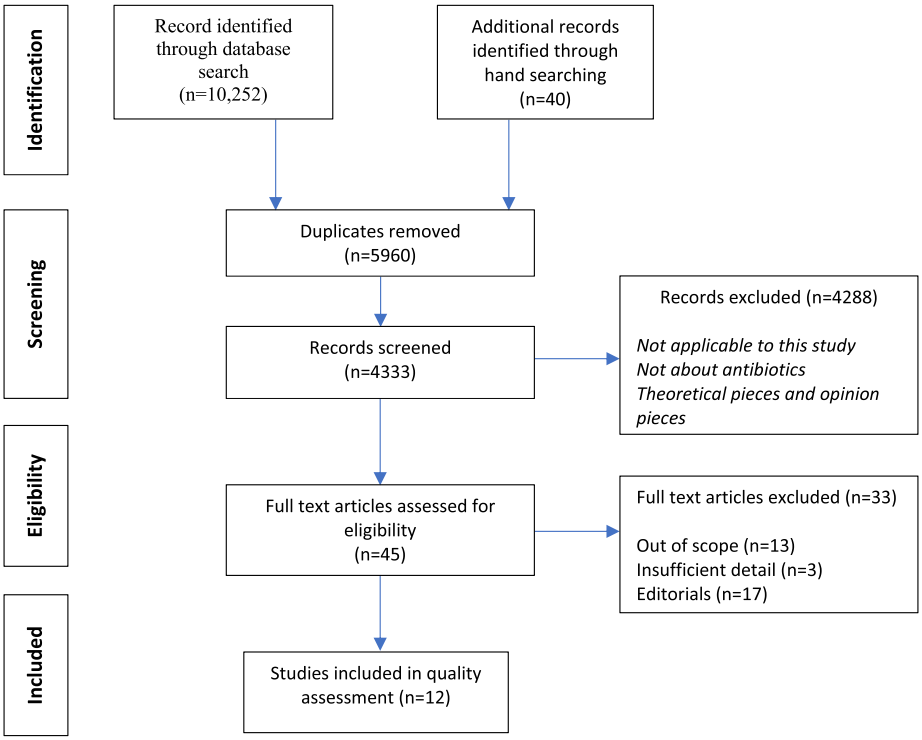

Fig. 1. Presents a Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR) flow diagram showing the process of searching and selecting the research articles.

study inclusion, were resolved through discussion. The total number of articles identified during the preliminary search was 10,252. After the removal of duplicates and the screening process in line with the predetermined eligibility criteria, twelve (12) articles were selected for analysis.

2.4. Data charting and synthesis

The data was extracted from the selected articles using a predesigned extraction sheet developed in Microsoft Excel. The information extracted into the adopted form included the citation, study type, study location, population, sample size, methods, forms of unwarranted antibiotic use, prevalence and COVID-19 associated reasons for antibiotic misuse. Two members of the research team conducted the data extraction, and the data chart was verified independently by another member of the team (Data charting: Additional file 3).

The selected studies were assessed for quality and risk of bias using the Mixed Methods Appraisal Tool (MMAT) version 28.[33]

2.5. Stakeholder consultations

Consultations with stakeholders were conducted as part of the six-stage methodological framework proposed by Arskey and O'Malley.[34] The consultations were held as a means of validating the study findings and contextualizing the study within the jurisdiction of study. The discussions also offered the additional advantage of communicating the findings of the review and creating the necessary foundation for the development of interventional strategies in line with advancements proposed by Levac.[35]

The stakeholders were purposively selected based on their institutional affiliation or position they occupied and the relevance to antibiotic stewardship and COVID-19 infection management. The professionals included doctors and pharmacists from the Ministry of Health, Food and Drugs Authority, academia, Pharmacy Council, Teaching Hospitals and the National COVID-19 Committee.

The participants were invited to partake in either a telephone interview or face-to-face interview. The time allotted for both interview formats were the same and lasted approximately ten (10) minutes using the same questioning guide. Stakeholders were asked open-ended questions centred on the utilization of antibiotics in the context of the COVID-19 pandemic. Participants reached via the telephone offered verbal consent whilst those reached via a face-to-face interaction signed an informed consent form for the interview. The consultative meetings were recorded and transcribed. Finally, the main thematic areas of the consultations were synthesized and categorized using the elements of the biopsychosocial framework.

2.6. Quality assessment of the included studies

The studies selected as part of the review were assessed for quality and risk of bias using the Mixed Methods Appraisal Tool (MMAT). The MMAT was a suitable appraisal tool for mixed studies reviews that include qualitative, quantitative, and mixed methods studies. All the included studies received a 'Yes' response in Part I of the MMAT checklist as a part of the prerequisite for selection. This implies that, all the selected studies had clear research questions and collected the requisite data to address these questions.

Part II of the MMAT appraisal was specific and tailored to the type of study. Amongst the included studies, only one study was qualitative in design and the remaining were quantitative.

The qualitative study met the entire MMAT checklist for qualitative studies. The majority of the quantitative non-randomized studies ($n = 3$) failed to account for the confounders in the study design and analysis. While an overall score from the ratings of each criterion was not calculated, most of the included studies met at least three of the corresponding specific MMAT criteria.

The summary of the MMAT quality assessment is presented in Additional file 2.

3. Results

3.1. Biological (clinical) factors

In this categorization, fever, dyspnoea and a productive cough were associated with antibiotic use for COVID-19 treatment[11,39] Other studies also demonstrated similar relationships between the use of antibiotics for COVID-19 treatment and clinical markers like a confirmed positive PCR test.[38,39,47] In the case of Baghdadi[38] et al., a study in the United States illustrated the likely overuse of Ceftriaxone (48.5%) and Azithromycin (46%) in treating COVID-19 hospital. in-patients not diagnosed with bacterial infection. Similarly, Van Laethem[39] et al. reported the unwarranted presumptive use of penicillin/beta-lactamase combinations for treating hospitalized COVID-19 patients in Belgium. The hospitalization of COVID-19 patients also appeared to be a basis warranting the use of antibiotics. In a study conducted in the Netherlands, the unwarranted use of antibiotics amongst hospitalized patients was reported, despite the low incidence of bacterial co-infections.[47]

3.2. Psychological factors

The fear of leaving home, going to crowded places and getting infected were reported to be enablers of antibiotic self-medication in a study conducted in Iran.[42] Similar patterns were observed in Nigeria where aside the fear of medical centres, participants also reported the fear of stigmatization, discrimination, quarantine and delays at the hospital.[44] In this regard, the anxiety resulting from the various COVID-induced fears had caused Nigerians to resort to self-medication for purported prophylactic reasons. The fear of death and infections coupled with the need to manage emotions in the context of the pandemic also contributed to inappropriate antibiotic consumption patterns.[46]

An Australian study seeking to explore the relationship between psychological distress and perceived health risks; also reported the cardinal role of COVID-19 associated psychological distress as an enabler of self-medication with antibiotics.[45] Perceived superiority of antibiotics as the perfect solution to inexplicable clinical infections also drove the inappropriate use of antibiotics for COVID-19.

Fear and the desire for patient compliance were amongst the several factors influencing the antibiotic dispensing patterns of healthcare providers during the pandemic. This resulted in the substantial dispensing of antibiotics without the requisite clinical indications and for longer durations than appropriate.[36]

3.3. Social factors

The preponderance of unwarranted antibiotic use as an antidote to the COVID pandemic was equally enabled by various structural factors such as, the congestion and delays in receiving treatment at medical centres.[44] Heydargoy[42] corroborated this observation by reporting COVID-induced fears generated from the crowding at medical centres.

The media plays a critical role in the social environment influencing unwarranted antibiotic use. For example, social media deliberations on the efficacy of taking antibiotics was a pivotal determinant on unwarranted antibiotic use.[46] Wegbom et al. also highlights the stress-inducing influence of the media in addition to the shortage of medicines, and stigmatization as external factors surrounding the inappropriate use of antibiotics.[44]

There were conflicting reports on the role of gender in the use of antibiotics during the pandemic. Oikonomou[48] reported a lack of association between gender and parents' attitude on antibiotic use for children in the course of the pandemic. However, Sadio[37] et al. records a correlation between being female and self-medication. The observation of females exhibiting a higher propensity to self-medication with antibiotics is equally reported in a study conducted by Wegbom[44] et al. in Nigeria.

Self-medication was also found to positively correlate with education and the professional affiliation as a health worker. Health professionals and people with a higher level of education were identified to most likely practice self-medication with antibiotics.[37]

3.4. Stakeholder consultations

Two (2) participants consented to a face-to-face interview and five (5) partook in a telephone interview. All the participants had at least a university degree and occupied focal positions relevant to the control, stewardship of antibiotics and COVID management. The participants represented the following institutions in Ghana: (i) Food and Drugs Authority, (ii) Ministry of Health, (iii) Pharmacy Council, (iv) Mental Health, (v) Academia, (vi) Quaternary Hospital and (vii) the National Guidelines for COVID-19 Committee.

Various themes emerged in the interview accounts of antibiotic utilization within the context of the ongoing COVID-19 pandemic. The thematic analyses was conducted in line with the six-step approach proposed by Braun and Clarke.[49]

Identifying the elements of the Biopsychosocial framework as the main thematic areas, the emerging themes were classified in accordance with this framework as summarized in Table 3 and narrated next.

3.5. Thematic results

Common to the various interview accounts were the issues of fear and anxiety driving the overuse, misuse, or abuse of antibiotics in the ongoing pandemic. Participants described the pandemic situation as a life and death situation which had no room for rational antibiotic use.

The fear and anxiety were not restricted to the lay community but also health workers at large. This resulted in a subtle disregard for rational assessment. A health worker commented; "*We all didn't seem to know what was working. If today we hear that Azithromycin is good, we would use it a bit more freely especially when we find that these antibiotics are safe.*" (Respondent 3).

"I recall my own COVID experience. I knew I didn't need antibiotics despite all my knowledge and what I have been telling people; I said, You know what, I'm coughing and the cough wasn't getting any better. Okay, the sputum has changed color so guess what, I went for antibiotics. Whether it made a difference or not. But definitely COVID has changed how people use antibiotics" (Respondent 6).

Another healthcare professional in justifying antibiotic supply remarked: *"We didn't know what we were fighting against, so antibiotics had to be given out. The state in which patients came in, we wouldn't want to wait for last minute before prescribing antibiotics. Also, we didn't have proper guidelines, everyone just wanted to* save *their patient."* (Respondent 7).

The confusion on clinically viable options resulted in antibiotic use not only for the perceived microbiological action but as a means of placating patient and health worker anxiety.

The weak regulatory system was another common factor propelling inappropriate antibiotic stewardship. A participant commented, *"And we know pharmacies are not regulated as effectively as we would wish they would. So, people can definitely go and get these antibiotics easily."* (Respondent 3).

The re-classification of some antibiotics from Prescription Only Medicine (POM) to Pharmacy Only Medicines was also described as a justification for unwarranted antibiotic access.

"There is unnecessary easy access to prescription only medicine. Now, Azithromycin has moved from prescription only medicine to pharmacy only medicine. You can buy without a prescription because of the COVID. And even before COVID, I am sure people could get it without a prescription." (Respondent 2).

All the respondents alluded to the existence of an AMR policy. However, some participants described this policy as impractical whereas others opined that the inability to implement this policy was the biggest hindrance to antibiotic stewardship.

"The existing AMR policy is not reflecting current practices and would need to be updated." (Respondent 7).

"It is an AMR policy and should include viruses/viral infections, but I don't think the AMR policy is positioned to handle a viral outbreak to the level of a pandemic." (Respondent 4).

"Existing AMR policy in Ghana. We need to review the existing AMR policy in Ghana and see if it is working or are we really working with it." (Respondent 5).

The nationally endorsed framework of antibiotic use in COVID management was also another issue reported as contributing to antibiotic misuse.

"There was this issue too, that well even though the evidence doesn't support *it, it is still in the treatment guidelines for Ghana. It wasn't in the WHO one, yet still Ghana adopted the routine use of antibiotics. For most*

Table 1
Characteristics of the included studies in this Scoping Review.

Article	Study Location	Study Design	COVID Diagnosis	Source of Antibiotic Misuse	Common Antibiotics Used	Factors associated with inappropriate antibiotic use
Elsayed et al.[36]	Egypt	Cross-Sectional (Questionnaires)	Unconfirmed (Presumptive)	Physician/Pharmacist Recommendation	- Azithromycin (40%) - Ceftriaxone - Linezolid	- Fear and seeking patient compliance
Estrada et al.[11]	Spain	Observational Retrospective Study	Confirmed	Doctor Prescriptions (Empirical)	- Beta-lactams (72.0%) - Macrolides (60.2%) - Fluoroquinolones (13.3%),	- Symptomatic profile of patient especially fever, dyspnea and a productive cough
Sadio et al.[37]	Togo	Cross-Sectional (Questionnaires)	Unconfirmed	Non-Prescription (Self-medication)	- Azithromycin (1.2%)	- Gender (Female) - Working in the health sector - Educational Level
Baghdadi et al.[38]	United States	Retrospective Observational Cohort Study	Confirmed	Doctor's Prescription (Overuse)	- Ceftriaxone (48.5%) - Azithromycin (46.0%) - Vancomycin (22.9%)	- First wave of the COVID-19 pandemic
Van Laethem et al.[39]	Belgium	Retrospective Quantitative Study	Confirmed	Doctor's Prescription	- Penicillin with beta-lactamase inhibitor	- Longer hospital stay - Presence of fever and low SpO2 - Pre-existing pulmonary disease
Karami et al.[40]	Netherlands	Retrospective Observational Cohort Study	Confirmed	Doctor Prescriptions (Empirical)	Second and third generation cephalosporins	
Akhtar et al.[41]	Pakistan	Retrospective observational study	Confirmed	Doctor Prescriptions	- Azithromycin (88.6%) - Ceftriaxone (23.6%).	
Heydargoy[42]	Iran	Online Questionnaire posted on all social networks of target group	Unconfirmed	Non-Prescription/ OTC	Not indicated	- Fear of leaving home - Fear of going to crowded places especially medical centres
Abdela et al.[43]	Ethiopia	Retrospective Cohort Study Design	Confirmed	Not indicated	-Amoxicillin/Clavulanate and Azithromycin (Most used oral antibiotics) - Ceftriaxone and Vancomycin (most used iv antibiotics)	Not Indicated
Wegbom et al.[44]	Nigeria	Web-based cross-sectional survey using a self-reported questionnaire	Not Indicated	Over the Counter	Not Indicated	- Fear of stigmatization or discrimination - Fear of being quarantined - Fear of contact with an infected person - Emergency illness and delay of hospital services - Gender - Educational attainment - Knowledge level on Self Medication
Zhang et al.[45]	Australia	Online Survey	Unconfirmed	Non-Prescription (Self-Medication)	Not Indicated	- Psychological distress associated with COVID-19 (panic and fear) - Lack of knowledge about the correct therapeutic role of antibiotics - Previous inappropriate use of antibiotics - Doctor-patient relationship
Kalam et al.[46]	Bangladesh	Qualitative telephone interviews	Confirmed (n = 20) and Unconfirmed (n = 20)	Non-Prescription (Self-Medication)	Not indicated	- Perceived superiority of antibiotics - Informal sources of treatment advice - Lack of access to COVID-19 testing and healthcare services - Dealing with social repercussions of symptoms, diagnosis, and isolation

other places you gave antibiotics when it was indicated i.e., when there is evidence of a bacterial infection. Because Ghana had adopted this routine use, people who hadn't tested positive but had the least cough, went in for antibiotics." (Respondent 6).

3.6. Stakeholder recommendations

- Educate prescribers more on the need practise targeted means of infection management.
- Ensure that nationally endorsed protocols for antibiotic usage are in line with evidence-based best practices.
- Address mental health issues during crisis of such nature: educate people on basic mental health strategies to deal with fear.
- Implement existing AMR policy.
- Simulate future public health emergencies and develop interventional strategies.
- Incorporate antimicrobial surveillance and resistance policy as a core part of the curricula in training health professionals.
- Review the AMR policy to meet the realities of clinical practice in Ghana.
- Increase public education on rational antibiotic use

4. Discussion

This review highlights several relationships between the custodial responsibilities and use of antibiotics in line with the ongoing COVID-19 pandemic (Table 1). Various studies have sought to establish the appropriate use of antibiotics in COVID-19 whilst highlighting the effectiveness and safety of antibiotics in Sars-Cov-2 treatment.[14,50–53]

However, not many studies have thoroughly examined the inappropriate use of antibiotics and the corresponding threat it poses to health security. In the context of the ongoing pandemic, the misuse of antibiotics can be characterized in many forms including the overuse of antibiotics, incorrect dosing, incorrect antibiotic combinations and wrong indications.[36] The few studies that sought to explore this upsurge of antibiotics misuse were mainly commentaries, opinion pieces and editorial letters which were excluded from the scope of this study[54,55,56,57,58,59]. This study does not only elucidate the misappropriate use of antibiotics but also presents the utilization of antibiotics vis a vis the social complexities of the ongoing pandemic.

The identification of the interplay between social factors and antibiotic use for COVID-19 is in line with the findings of Toro-Alzate, Hofstraat, & de Vries, (2021) in their study of the social relationships between COVID-19 and antimicrobial resistance based on the SPECIAL SOC AMR Framework. This current scoping review using the Biopsychosocial model has illustrated the inappropriate utilization of antibiotics through the lens of a biological (clinical), social and psychological categorization (Table 2).

The geographical representation of the included studies is sparsely distributed across a wide region (Egypt, Bangladesh, Spain, Togo, United States, Belgium, Netherlands, Greece, Pakistan, Iran, Ethiopia, Nigeria, and Australia). The scarcity of primary studies that outline the enablers of antibiotic misuse as a coping strategy to the COVID-19 pandemic is evident. Approximately 67% of the included studies were from the African and European Region. The studies within the European region were retrospective in design and could not comprehensively identify the factors associated with the misuse of antibiotics. The study conducted by Baghdadi et al. in the United States also exhibited a similar profile to that in the European region.[38] These are developed settings with robust data systems which may explain the feasibility of the identified retrospective data reports. Trends in the African region as evidenced from studies by Wegbom et al. (2021) and Sadio et al. (2021) mostly reflected the non-prescription use of antibiotics as a means of self-medication. This could be attributed to the relatively weaker regulatory structures facilitating the unlicensed access to prescription medicines in Africa.[61]

Table 2
Key findings following the Biopsychosocial framework.

Results (Factors)	Sub-themes	Biopsychosocial Theme
- Symptom profile suggesting COVID infection. - Presence of a fever - Positive PCR test for COVID-19 - Presence of co-morbidities. - Hospital Admission - Wave of COVID-19 pandemic - Prescription practices of General Practitioners encouraging antibiotic hoarding	Clinical signs and symptoms, laboratory markers, medical protocols	Biological (Clinical)
- Fear of infection or contact with an infected person - Fear of crowds and infections at medical centres - Fear of being quarantined - Stigmatization or Discrimination - Emotional anxiety - Social repercussions of symptoms, diagnosis, and infection - COVID-19 associated psychological distress - Fear and desiring patient compliance - Perceived superiority of antibiotics as the ultimate solution	Anxiety, fear, perceptions	Psychological
- Uncertainty and difficulty in accessing COVID-19 and microbiological tests - Career in the health sector - Delays receiving hospital services - Distance to the health facility - Knowledge of antibiotics - High School Education or higher - Experiences in using antibiotics - Relationship with doctors - Gender (Female) - Influence of media - Informal sources of treatment advice - Medicine shortages	Education, legislation, health systems, gender, career, peer pressure, community structures, media	Social

Azithromycin was the most common antibiotic used as a prophylactic and curative means of managing COVID-19 infections. This may be due to its reported potential antiviral and anti-inflammatory properties.[62] Trends of increasing azithromycin overuse during the pandemic especially as a result of media posts were also reported by Bogdanić, Močibob, Vidović, Soldo, & Begovać, (2022). Despite the promising evidence supporting the use of Azithromycin as a prospective therapeutic agent for COVID-19, concerns are raised on the widespread unreasonable antibiotic therapy in COVID-19 patients.[64]

Despite the established clinical basis for antibiotic utilization, the use of antibiotics in this context characterized as unwarranted or misused is as a result of various factors. These include clinical markers such as the existence of co-morbidities,[39] productive coughs[65] and a fever.[39,65]

Beyond clinical signs, noteworthy is the psychological distress associated with the COVID-19 pandemic which enabled trends of substance or medicines abuse.[66] Substance abuse which can also be characterized as self-medication is a common coping strategy adopted by individuals experiencing a form of psychological distress.[67] The resultant effects are various health and social implications for a huge number of individuals.[68]

Table 3
Stakeholder thematic results characterized by the Biopsychosocial framework. Factors (enablers) of Antibiotic Misuse for COVID-19 Management

Biopsychosocial Theme	Sub-theme	Explanation
BIOLOGICAL (CLINICAL)	Drug Repurposing	The repurposing of already existing drugs such as antibiotics justifies its sporadic use.
	Confusion on viable clinical options	In the absence of any other viable clinical antidotes to COVID, antibiotics are used not only for a microbiological action but also a placebo effect.
	Antibiotic Cocktails	People were combining different antibiotics or modifying antibiotic dosing schedules as a curative approach to COVID-19.
	Perceived Safety of Antibiotics	Antibiotics are safe and there is no harm taking it even when you are unsure about the COVID infection.
PSYCHOLOGICAL	Heightened Fear	The fear of infection surrounding the pandemic motivated the use of antibiotics as an antidote.
	Anxiety	People were anxious with the least symptom mimicking a cough or cold. Antibiotics acted as anxiolytics in this regard.
	Treatment Panic	The reports of COVID-related deaths created a sense of panic which resulted in the non-rational use of antibiotics as a kneejerk reaction.
SOCIAL	Treatment Publicity	Widespread publicity of COVID treatment protocols reinforced public decision to use antibiotics for self-medication.
	Weak Regulatory System	Pharmacies are not regulated as effectively as required. Hence, the creation of an unwarranted access pathway to antibiotics.
	Drug Classification	Antibiotics such as Azithromycin have moved from prescription only medicine to pharmacy only medicine. Hence, can now be bought without a prescription because of the COVID
	Azithromycin Hype	The social hype about Azithromycin characterizes it as a COVID wonder drug.
	Public Knowledge Deficit	Most people are unable to differentiate between a bacterial infection and a viral infection. COVID is an infection, so they treat with antibiotics.
	Weak AMR Policy Implementation	The AMR policy is not well positioned to address current practices in antibiotic utilization and is currently facing challenges in implementation.
	Economic Incentives	Pharmacy business owners found an opportunity to cash in with the sale of antibiotics.
	National Endorsement	Not entirely in line with evidence-based practice, Ghana made routine antibiotic use a core part of their COVID management protocol.
	Media Influence	Media especially social media was awash with so many things including antibiotics that were purported to help people recover or even prevent COVID.

These patterns of self-medication do not differ significantly from the trends of substance use as a result of anxiety disorders. The self-medication hypothesis is posited as a common explanation for the observed comorbidity of anxiety disorders and substance use disorders.[69] This hypothesis posits that, individuals with mood or anxiety disorders will use substances to cope with the difficult symptoms prevailing at that time. Nevertheless, the psychological disposition influencing the misuse as a coping strategy to the pandemic is not restricted only to the antibiotic user but also the suppliers of antibiotics as evidently corroborated by the stakeholder consultative discussions.

The health system structure, delays at the hospitals and socio-economic implications have also been reported as established determinants of self-medication.[70–72] This mimics the current observed trend of unwarranted antibiotic use in response to the external factors such as, the congestion and delays in receiving treatment at medical centres.[44] Most especially in low- and middle-income countries (LMICs) where the inadequacies of a resource-constrained healthcare environment contribute strongly to the different and emerging factors associated with the non-prescription use of antibiotics.[73,74]

Beyond health systems, the stress-inducing influence of the media coupled with challenges such as shortage of essential commodities and stigmatization are also determinants underpinning the inappropriate use of antibiotics.[44] Generally, the COVID-19 pandemic has created a seemingly hostile social environment that triggers a turmoil of distress as well as a myriad of considerable fears.[75,76] The COVID-19 related media reportage is a critical aspect of this hostile environment and that unearths inexplicable anxieties, depression and fears.[76]

The role of gender in enabling the misuse of antibiotics cannot be excluded in the social categorization of this review. The association between being female and self-medication is not foreign to existing literature. Carrasco-Garrido in offering a gender perspective on self-medication in Spain reports a prevalence of self-medication amongst women superseding that of men.[77] This reported trend may be explained by the preponderance of females demonstrating greater fear and anxiety than their male counterparts.[78] These fears and anxieties have heightened amongst women in the context of the ongoing COVID-19 outbreak.[79,80]

Self-medication was also found to positively correlate with education and the professional affiliation as a health worker. Health professionals and people with a higher level of education were identified to most likely practice self-medication with antibiotics.[37]

Conclusively, the observations of this review correspond with that of Buckner et al. in a study outlining the biopsychosocial model of social anxiety and substance use.[81] In their study, chronically elevated negative affective states and fear of scrutiny were aspects of social anxiety working in concert to place vulnerable individuals at risk for substance use.[81] In the case of this study, the multiple reported fears and anxieties characterized by the novel coronavirus pandemic coupled with biological indicators ambiguously suggesting an infection and social impediments such as hospital congestions have resulted in the inappropriate supply and use of antibiotics as a coping strategy to the pandemic.

5. Limitations

Common to the limitations of the Biopsychosocial model, the degree of influence exerted by each component of factors whether biological, social, or psychological is unaccounted for. The majority of the cross-sectional studies included in this review were conducted using web-based or online platforms which skewed respondents towards those who were educated and/or belonging to an economic class capable of affording an internet-enabled phone from which data were collected. Despite these limitations, this review has shown that interventions such as policies, guidelines and strategies targeted at the control of antibiotics in the course of the COVID-19 pandemic and future pandemics should simultaneously address the three major thematic areas of the biopsychosocial model while taking into cognizance country-specific peculiarities. In addition, including the stakeholder consultations as part of this review also highlighted key clinical practice and policy perspectives to the review findings on the use and misuse of antibiotics during the COVID-19 pandemic.

6. Conclusion

As maintained by the biopsychosocial model, the COVID-necessitated use of antibiotics is a result of an extensive interplay of social, psychological, and biological (clinical) factors. The pandemic-enabled determinants of unwarranted antibiotic use common to the review and stakeholder consultations include fear, emotional anxiety, media influences and public knowledge deficits. The stakeholder consultations also outlined critical issues such as the need to evaluate the effectiveness of the antimicrobial policy, the importance of mental health in pandemics and the national call to action for evidence-based medical practice despite prevailing anxieties. The study findings serve as the basis for further research into the sociocultural and psychological enablers of inappropriate antibiotic use as a rationale for developing targeted and comprehensive policy interventions in antibiotic stewardship.

Authors' contributions

RAN designed the study, screened the studies, searched literature, appraised the quality of the papers, conducted the stakeholder consultations, analyzed the data, and drafted the manuscript. IAK screened the studies, analyzed the data, and supervised the study. AK appraised the quality of the papers, analyzed the data, and revised the manuscript. KOB revised the study design, revised the manuscript, and supervised the study.

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Declaration of competing interest

None.

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Appendix A. Supplementary data

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