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Evaluating Antibiotic Stewardship at a Tertiary Care Hospital in Kerala, India

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Abstract

Objectives: To conduct interviews with healthcare professionals to determine what barriers and facilitators to antibiotic stewardship existed within their facility.

Setting: 1300 bed tertiary care private hospital located in the state of Kerala, India.

Participants: 31 semi-structured interviews and 4 focus groups with hospital staff ranging from physicians, nurses, pharmacists, and a clinical microbiologist.

Results: Key facilitators of AS at the hospital included a dedicated committee overseeing appropriate inpatient antibiotic use, a highly capable and prompt microbiology lab, a high level of AS understanding among staff, established guidelines for empiric prescribing, and an easily-accessible antibiogram. We identified the following barriers: limited access to clinical pharmacists, physician immunity to change regarding stewardship policies, infrequent antibiotic de-escalation, high physician workload, an incomplete electronic medical record (EMR), inadequate ASP physical visibility, and high antibiotic use in the community.

Conclusions: Opportunities for improvement at this institution include increasing accessibility to clinical pharmacists, implementing strategies to overcome physician immunity to change, and establishing a more accessible and complete EMR. Our findings are likely to be of use to institutions developing ASPs in lower resource settings.

Keywords: Antibiotic stewardship, antibiotic stewardship programs, antibiotic resistance, India, SEIPS

Strengths and limitations of this study

- Our study is the first of its kind to systematically examine the key barriers and facilitators of implementing an ASP in a LMIC.
- We interviewed a variety of healthcare workers: physicians, nurses, clinical pharmacists, and a microbiologist.
- This was a single center study. Thus, transferability of our findings to more resource-limited rural hospitals within India or to other LMIC may not be possible.
- We did not conduct direct observations of practice to correlate with self-reporting.

BMJ Summary Box

What is already known?

- Antibiotic resistance is a growing area of concern in healthcare settings around the world, and LMIC often face disproportionately high rates of resistant infections
- Antibiotic stewardship programs have been found to help foster judicious antibiotic use.

What are the new findings?

- Our study is the first of its kind to systematically examine the key barriers and facilitators of implementing an ASP in a LMIC.
- Facilitators include a proactive ASP with committed leadership, highly capable and prompt microbiology lab, broad understanding of AS concept among staff, easily accessible antibiogram, and established guidelines for empiric prescribing
- Barriers include limited access to clinical pharmacists, physician immunity to change, high physician workload, lack of antibiotic de-escalation, incomplete EMR, inadequate physical visibility of stewardship activities, and widespread community antibiotic use

What do the new findings imply?

- The careful design of ASP with consideration to overcoming barriers and strengthening facilitators will improve antibiotic use and curve the spread of resistant organisms.
- Hospitals in LMIC should invest in ASP with consideration to variables which are easily implemented and cost effective in their unique setting. Launching and sustaining a new program will be more feasible if hospital leadership is supportive and the stewardship team meets daily to discuss cases.

Background

The United Nations declared antimicrobial resistance to be "the greatest and most urgent global risk" in 2016[1]. Antibiotic overuse and misuse drives antimicrobial

resistance[2]. Antibiotic resistant infections frequently occur as healthcare associated infections, and most deaths from antibiotic resistance take place in inpatient healthcare settings[3]. In developing countries, the risk of contracting an antibiotic resistant healthcare-associated infection may be two to 20 times higher than in developed countries[4]. This discrepancy is likely due to factors such as over prescribing and the widespread availability of antibiotics without prescription[5,6]. The same situation exists in India, where rates of infections caused by antibiotic resistant bacteria are high and increasing[7-15]. Given that the main driver of antibiotic resistance is antibiotic use and misuse, antibiotic stewardship (AS) and antibiotic stewardship programs (ASP) have a critical role in promoting judicious antibiotic use[16].

In a recent review of ASP international programs, Davey et al. found ASPs were effective in decreasing treatment duration and increasing adherence to antibiotic use policy[17]. While the evidence for ASP effectiveness is growing, there is considerable variation among ASPs in size, activities, and scope. Newly published consensus of an ASP core elements checklist includes experts from twelve countries on six continents and is suitable for LMIC[18].

Low and middle income countries face ASP implementation challenges including limited diagnostic lab capability, inadequate awareness, limited access to quality antibiotics, and high patient census[19]. To date, few studies have explored the challenges facilities in India face carrying out ASPs, such as less available manpower and money dedicated to maintaining a detailed electronic medical record (EMR)[20-22]. We selected India because, as mentioned, antibiotic resistance rates are high and increasing, and our study facility had recently implemented an ASP to address this issue. Thus, we undertook a

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prospective study in Kerala, India to examine the barriers and facilitators to practicing AS in a LMIC healthcare setting and to identify opportunities to improve AS.

Methods

Location

In January 2018, we conducted a qualitative study to understand the barriers and facilitators to AS at a 1300 bed tertiary care private hospital located in the state of Kerala, India. This hospital, which includes 275 intensive care beds, provides free or subsidized advanced care for two-thirds of its patient population. The hospital's ASP, which includes clinical pharmacists, physicians, and a medical microbiologist, began in 2016.

Study population

Physicians, nurses, clinical pharmacists, and a microbiologist were identified using purposive sampling by the on-site study team. A study team member emailed information to staff regarding the project and subsequently approached staff in-person to identify interested participants. We included senior faculty and healthcare professionals working on the critical care medicine and infectious disease teams for interview. Interviews were conducted until theoretical saturation. Exclusion criteria included non-English speaking staff and staff who were subordinates to any member of the study team.

Data collection

We conducted 31 semi-structured interviews and 4 focus groups with hospital staff involved in AS. Interview guides were developed based on the Systems Engineering Initiative for Patient Safety (SEIPS) framework. This framework evaluates the interactions between the people, organization, tasks, tools/technology, and environment of a given work system, allowing for identification of key areas for improvement or intervention[23].

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Interviews were conducted in private rooms at the hospital, and were audio recorded after obtaining verbal consent from the participant. No personal information was recorded, and each interview lasted between 10 and 30 minutes. Interview guides (Appendix A) were continuously revised to uncover novel information.

Analysis

All interviews were transcribed and analyzed deductively using the SEIPS framework. One member from the study team manually coded the interview transcripts. Quotations from transcribed interviews were sorted into the SEIPS categories of person, organization, tasks, tools/technology, and physical environment. After all study team members agreed on the identified themes from the interviews, the most prominent barriers and facilitators to AS were identified in each category based on number of participant responses. We used the SRQR reporting guidelines[24].

Ethics approval

The Institutional Review Board at the University of Wisconsin-Madison granted this study exemption from full review. The Internal Ethics Committee at the participating hospital reviewed the study and granted approval.

Patient and Public Involvement statement

The development of our study was informed by many patients' preference to get antibiotics right away, just in case these drugs help. This can influence how healthcare providers deal with prescribing. We did not involve patients with the design or conduct of the study. Results will be disseminated to the involved healthcare workers at staff meetings and electronic communications.

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Results

In total, we interviewed 45 hospital faculty and staff. Participants included individual interviews with physicians (27), clinical pharmacists (3), and one microbiologist. We also conducted four focus groups consisting of ASP team members, pharmacists (two groups), and infection control nurses with two to five participants each.

Organization

The hospital's ASP is the key organizational component of promoting judicious antibiotic use. This team, led by a physician and comprised of physicians, clinical pharmacists, and a medical microbiologist, evaluates the list of inpatients receiving antibiotics to evaluate "The Five R's" of antibiotic prescribing: right drug, right dose, right frequency, right duration, and right indication. When the team identifies opportunities for antibiotic de-escalation or reduced duration, a clinical pharmacist member contacts the prescribing physician to issue treatment recommendations, and the prescribing physician decides whether to modify treatment. This program frequently communicates with staff via email and offers an annual AS symposium. Moreover, according to about half of respondents, hospital administrative leadership champions the ASP. Staff identified this robust program as a key facilitator of AS at the hospital (Table 1, quotes 1-3).

In addition to a highly capable ASP, 17 interviews (48.6%) regarded the microbiology lab as a key facilitator of AS. Staff praised the 24-hour lab's promptness and the rapidity with which lab staff uploaded results into the EMR. In addition, many physicians relied on the microbiologist's expertise for help identifying microorganisms in complicated infections (Table 1, quotes 4 and 5).

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Despite having an effective stewardship program and lab, 16 interviews (45.7%) identified limited clinical pharmacist availability as a barrier to AS. Many physicians recognized clinical pharmacists' knowledge as a critical component of patient care. However, several departments had one clinical pharmacist and many had none at all. Staff worried this lack of pharmacist access may cause clinicians to miss drug interactions or prescribe antibiotics at incorrect dosages (Table 1, quotes 6-8).

Person

A majority of participants (57.1%) displayed knowledge of AS concepts, policies, and practices during our interviews. Staff identified AS activities, such as using the correct antibiotic at the correct dose, as a key component of reducing antibiotic resistance. In addition, staff mentioned they often heard about AS at work. This high level of awareness among staff facilitates AS practices (Table 1, quotes 9-11).

While most interviewed staff demonstrated AS policy understanding, they revealed many physicians resisted accepting suggestions from the ASP. Moreover, several physicians and pharmacists worried other physicians did not acknowledge pharmacists' contributions to patient care. According to nine interviews (25.7%), this immunity to change may impede AS practices and contribute to antibiotic resistance through incorrect antibiotic dosing and duration (Table 1, quotes 12 and 13).

Tasks

Staff in 12 interviews (34.3%) felt that clinicians follow established guidelines when prescribing antibiotics when the cause of illness is not yet known. Following a clinical evaluation, the physician orders a culture and initiates a broad-spectrum antibiotic. Physicians then use this culture result to modify the original antibiotic used. This process,

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often called de-escalation, involves selecting an antibiotic which has a more specific spectrum or stopping antibiotic treatment if the cultures do not identify a bacterial infection (Table 1, quote 14).

As a tertiary care facility, this hospital frequently treats high-risk patients who have acquired resistant infections in the community or at other hospitals. Therefore, physicians at our study institution often feel compelled to empirically prescribe broad-spectrum antibiotics while awaiting culture results. However, physicians often forget or refuse to de-escalate antibiotic use due to workload or fear of losing the patient. In our study, physicians and pharmacists in eight interviews (22.9%) worried this lack of de-escalation may increase the risk of antibiotic resistant infections (Table 1, quote 15) and cited de-escalation as the most important issue regarding antibiotic prescribing. Similarly, in nine interviews (25.7%), staff members feared their high workloads may negatively impact their ability to always judiciously prescribe antibiotics. Physicians noted they are often unable to spend sufficient time evaluating a patient or recall pre-admission drugs, thus leading to antibiotic over-prescription (Table 1, quotes 16 and 17).

Tools/Technology

The hospital microbiologist and clinical pharmacists update the hospital antibiogram annually. The antibiogram, which gives the percent of pathogens susceptible to various antimicrobial agents, is accessible on the hospital intranet and divided into Gram positive, Gram negative, and yeast. In 17 interviews (48.6%), staff members identified this user-friendly tool as a key facilitator in selecting antibiotics based on hospital resistance patterns, a critical component of AS (Table 1, quote 18).

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In addition to the antibiogram, this hospital also utilizes an EMR to store information on inpatients, a useful addition for identifying immediate drug interactions and thereby reducing harm. However, the EMR does not contain a patient's full scope of antibiotic use, including antibiotic history, duration, and dose. This incompleteness often forces physicians and pharmacists to refer to a patient's paper health record, which one pharmacist described as a "tedious" process. Moreover, physician workflow does not include entering antibiotic data into the EMR. Due to high work volume, physicians depend on the ward secretary, nursing assistants, or research assistants to update the EMR. In 12 interviews (34.3%), staff members identified this inability to quickly access the full scope of a patient's antibiotic history as a barrier to judiciously prescribing antibiotics (Table 1, quotes 19 and 20).

Environment

Despite having a highly engaged AS team, staff mentioned the hospital did not have signs or posters to increase stewardship awareness, which several staff identified as a potentially useful addition. A few interviewees thought AS policies were sometimes printed and posted but did not "stand out." These printed antibiotic prescribing protocols were not visible to all staff, and in 23 interviews (65.7%) staff members mentioned this limited visibility may inhibit widespread AS awareness. (Table 1, quotes 21 and 22)

In addition, staff identified high local antibiotic use as a barrier to stewardship. As patients can purchase antibiotics over the counter or have been recently hospitalized at another facility, many patients enter the hospital already using antibiotics. These high use rates often lead to antibiotic resistant infections in the community, forcing physicians to prescribe broad-spectrum antibiotics. Furthermore, several staff feared the impact of high

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antibiotic use in animal husbandry and fisheries on spreading resistance. In 7 interviews (20%), staff members wished for enhanced antibiotic prescribing regulations and more AS awareness in greater India (Table 1, quote 23).

Discussion

Our study is the first of its kind to systematically examine key barriers and facilitators of implementing ASP in a LMIC tertiary hospital. Using the SEIPS model, we examined the implementation of an ASP at a large tertiary care hospital in order to identify opportunities to improve this program.

We found that limited access to clinical pharmacists, physician immunity to change resulting in infrequent antibiotic de-escalation, high physician workload, an inadequate EMR, inadequate physical visibility of stewardship activities, and high antibiotic use in the community were major barriers to effective ASP implementation. The presence of a proactive ASP with committed leadership, highly capable and prompt microbiology laboratory, high level of understanding of AS among staff, easily accessible antibiogram, and established guidelines for empiric prescribing were identified as important facilitators of an effective ASP in this hospital.

Our study found limited access to pharmacists was a barrier for an effective ASP. Multidisciplinary rounds with guideline-based antibiotic recommendations for specific infections have been found to decrease use and duration of both broad spectrum and high-end, reserve antibiotics[25]. Clinical pharmacists can provide real-time decision support which could significantly improve rates of antibiotic tailoring to culture data[26]. Empowering clinical pharmacists to identify highly misused antibiotics, design guideline-

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based de-escalation protocols, and participate in multidisciplinary rounds may improve the quality of ASP.

Physician resistance to changes in antibiotic use practices was identified as a barrier to an effective ASP. Factors which influence physician antibiotic prescribing habits include anxiety about missing an infection and the antibiotic prescribing behavior of peers[27]. This is an important active area of research; interventions such as encouraging reflection on practice, the use of audit and feedback, small-group learning with discussions and engagement by senior clinicians, and deploying multidisciplinary teams including clinical pharmacists have been shown to improve prescriber behavior[28,29]. In LMIC settings, we recommend leadership should actively promote ASP activities and their value. Feedback on antibiotic usage and patterns should be disseminated to improve adherence to local or national guidelines at this facility.

We found that the usability and accessibility of the EMR were another barrier to an effective ASP. Adoption of an EMR can improve ASP by providing microbiology results, radiology studies, and clinical data[30]. These factors allow ASPs the opportunity to further curtail antibiotic use; our data here support these findings. However, the expense of acquiring and optimizing an EMR system to harness its full potential makes this intervention difficult to implement, particularly in LMIC settings[31].

Our study identified high and indiscriminate community-based antibiotic use as a barrier to practicing AS at our study site. Variably-enforced regulations on antibiotic dispensing and the availability of antibiotics without a prescription is a widespread problem in many countries, including India[32]. The broad and unregulated use of antibiotics in animal feed and fisheries compounds this barrier[33]. ASP in healthcare settings can be

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complemented by AS in the community for all uses of antibiotics, with an inclusive "One Health" approach to addressing resistance[34].

Our study has limitations. First, this was a single center study. Thus, transferability of our findings to more resource-limited rural hospitals within India or to other LMIC may not be possible. Second, we did not conduct direct observations of practice to correlate with self-reporting. Future studies may identify additional barriers and facilitators by implementing direct observation approaches to collect data on stewardship practices.

Conclusion

The use of the SEIPS model to analyze an ASP in an LMIC identified barriers and facilitators within the healthcare work system. Opportunities for improvement at this institution include increasing accessibility to clinical pharmacists, implementing strategies to overcome physician immunity to change, and establishing a more accessible and complete EMR. Interventions which account for and address barriers and strengthen facilitators should be tested in future studies for their effect on antimicrobial usage and resistance.

Author Statement

KB created the interview guides, conducted in-person interviews, and wrote, edited, and prepared the manuscript. CS created the interview guides, conducted in-person interviews, and wrote/edited the manuscript. JK edited the manuscript. LK conducted on-site data collection and wrote/edited the manuscript. MVJ assisted with on-site data collection and edited the manuscript. SS devised the project and edited the manuscript. NS obtained

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Table 1. Themes identified from SEIPS components with corresponding representative quotations

Theme	Representative Quote
Organization	
Antimicrobial Stewardship Program	1. "We audit to make sure the right indication is happening. We check to see the dosage is correct and monitor what's happening here to track our prescriptions." (pharmacist)
	2. "Every year we do something with the antibiotic prescription program. Along with infection control. Usually a three-day program for doctors and one day is dedicated to antibiotic stewardship. Speakers from all over the country [come] and we take about 30-35 doctors a year and try to teach them about antibiotic stewardship." (infection control nurse)
	3. “The medical superintendent is a part of our team. I don’t think you can get much higher up than that. The management is very supportive.” (pharmacist)
Microbiology laboratory	4. "Our microbiology lab is one of the best in the country. They are very reliable and help us immensely." (physician)
	5. “Whenever the lab grows something in the culture, could be six hours, ten hours, we are called and told. So that does impact our management. If we are thinking about a gram positive illness and we get a culture that’s gram negative, which is grown very quickly, we totally change our report. We are informed pretty quickly.” (physician)

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Clinical pharmacist availability	6. "[Pharmacists are] not routinely in the ICU. I wish more pharmacists would tell physicians their doses or their drug interactions are wrong, but I don't see them in the cardiac or pediatric ICU." (physician)
	7. "We have one pharmacist in our ICU, she visits. The problem with her is she's overworked. She's alone. She comes on the rounds only sometimes and comes around and checks the antibiotics dosing is correct. But duration and all others are decided by physicians. If there were more of them it would be much better." (physician)
	8. "If a clinician is working alone, we may not have much concern about things that pharmacists are more aware of, like drug interactions. Routine medications may have interactions also, so pharmacists' help is needed. That type of information is more with the pharmacists, not the clinicians. They are not always available." (physician)
Person	
Antibiotic stewardship knowledge	9. "Antibiotic stewardship is a standardized practice with the right treatment at the right time." (physician)
	10. "To me antibiotic stewardship is to start judicious antibiotics…I won't say to start low antibiotics, I say to start optimum antibiotics." (physician)
	11. "Most of us here are aware of these ideas. For us, it's about everything that has to do with a prescription. The ultimate aim is judicious use of antibiotics. We need to use the right antibiotics, the right dose." (physician)

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Physician resistance to antibiotic stewardship policies	12. "I think clinicians are empowered to think that they know best. They need to recognize the roles of the microbiologists and the pharmacists and should not feel low that they have asked for help." (physician)
	13. "Challenges come from navigating human behavior. Sometimes you'll recommend things but people just won't listen to you." (infection control nurse)
Tasks	
Antibiotic prescribing	14. "We have a high patient load and socioeconomic status is a big deal. Poverty and malnourished children are a reality. We can't wait for cultures. We have protocols to start them on antibiotics according to which ones have been most successful here." (physician)
	15. "I think it's a problem all over India, because the first antibiotics they prescribe is the carbapenems. And once they prescribe it is never de-escalated or rarely de-escalated. Basically they go, 'let's continue. What the culture says? I don't want to do that. Let's just continue because he's improving.' So it's a major, major, major problem." (physician)
Workload	16. "Sometimes we are busy and we forget pre admission drugs which are missed because we are more worried about the current problems and there are so many the patient is already on that we need to continue." (physician)
	17. "Our work here does affect how long you can spend on individual cases." (infection control nurse)

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Tools and Technology	
Antibiogram	18. "It is an annual antibiogram. We divide it into gram positive, gram negative, and yeast. We also have a blood gram positive from blood isolates, negative, and yeast. They are separate. We follow international guidelines so for any isolate that is more than 30, we take them and follow the rules. Every year it is updated. This year they are trying to involve more pharmacists" (infection control nurse)
Electronic medical record	19. "If I look today at the record, I can only see what they took today. The current medications only. Not what they got yesterday. I can't trace the meropenem. To see all the drugs we have to go to the paper medical record room. It's a very tedious process. We don't know the dose or duration or all the drugs…if the patient returns in a few weeks, we don't know what they were taking and what will be effective." (pharmacist)
	20. "I see 80 patients a day. So it's not possible for me to spend so much time logging in, recording all this. I don't think it's possible unless I had someone sitting next to me doing just that." (physician)
Environment	
Posters or signs promoting antibiotic stewardship awareness	21. "It's only in protocols, which we do print out only for doctors. Nurses don't see that." (physician)
	22. "We have some print-outs on our notice board about colistin and other higher-end antibiotics…but we don't have posters. As for the printouts, they aren't that catchy." (physician)

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High levels of community antibiotic use	23. "Outside the hospital this is a rampant problem in India. There is much abuse and misuse of antibiotics. Anyone can just go to a roadside pharmacy and describe their symptoms and get antibiotics over the counter just like that. They just go to the guy sitting there and get whatever. I think we should make it much harder to get antibiotics." (physician)

Frequently used abbreviations:

LMIC: low and middle income countries,

ASP: antibiotic stewardship program,

AS: antibiotic stewardship,

SEIPS: Systems Engineering Initiative for Patient Safety,

EMR: electronic medical record

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Appendix A: Antibiotic Stewardship Interview Questions

Interviewer: Antibiotic stewardship refers to the judicious use of antibiotics, and is a critical component of reducing antibiotic resistance. Components of antibiotic stewardship involve drug expertise, evaluating ongoing antibiotic treatment, monitoring prescribing practices, and reporting information on antibiotic use and resistance.

Your responses will be recorded with a voice recorder and transcribed, but the responses will be de-identified in any data set and your identity will be kept confidential.

Person

1. How do you define antibiotic stewardship?
2. What do you think of antibiotic stewardship as an infectious disease prevention strategy?
3. Describe your level of interaction working with infectious disease specialists at your hospital.
4. Physician/Nurse
    a. Describe your work with pharmacists in your hospital.
        i. If poor availability/they don't work with pharmacists: What factors limit their availability to you?
        ii. How do you work with pharmacists on specific patients?
        iii. In an ideal situation, what would be different about how you work with the pharmacists?
    b. Tell me about your workload.
        i. How does your workload impact your ability to complete your job responsibilities?
5. All clinicians: Describe employee turnover on your ward

Organization

1. Describe your experience regarding antimicrobial stewardship education in your facility.
    a. What is your view of these trainings (how likely are you to attend? Do you apply the information to your practice? Who attends?)?
2. What do you hear about antimicrobial stewardship at work?
3. Describe a time a new policy was implemented on your ward/in your lab.
    a. What challenges were encountered? What went well? How did this compare to other times when new policies were implemented?
    b. How were staff involved in the development of the new policy? How are they typically involved in policy development
4. Tell me about your interactions with people involved in the antibiotic stewardship program.
    a. What types of things do you collaborate on/communicate about?
    b. How could your interactions be improved?
5. What is your sense of how hospital leaders/management are involved in antibiotic stewardship efforts in your ward/lab?

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6. All clinicians: How could antibiotic prescribing be improved in your facility? Tell me about empiric prescribing at your hospital. What factors should be considered when prescribing an antibiotic if the cause of illness is not yet known?

Tasks

1. Lab Staff
    a. Describe how you create an antibiogram.
        i. How does creating an antibiogram fit in with your other job responsibilities?
        ii. How often do you update the antibiogram?
        iii. What is the scope of the antibiogram?
2. Nurses
    a. What antibiotic stewardship practices are you responsible for on your ward?
    b. How often do you review medications? Describe your review process.
    c. What do you do when antibiotic usage seems questionable? Do you or your team decide together?
    d. Are routine audits of antibiotic use conducted on your ward?
3. Pharmacists
    a. What is your process when an antibiotic is ordered?
        i. What are your selection review practices? Describe your collaboration with physicians.
        ii. Describe your antibiogram use, including successes and challenges. How frequently is it updated?
4. Physicians
    a. Describe your antibiotic selection process, including any guidelines you may use in making your decision.
        i. Describe your antibiogram use, including successes and challenges. How frequently is it updated?
        ii. How often are those guidelines adhered to in your workplace? If infrequently, what are the barriers to adherence?
    b. Describe your review of antibiotic selection, including after the drug has been prescribed and after you have obtained culture results.
5. All clinicians: Where do you store information on antibiotic use (dosage, duration, indication)?
6. All clinicians: How often/how many cases of treatment failure related to resistance have you seen?
7. All staff: Evaluate the effect of your workload on your ability to implement antibiotic stewardship activities.
8. Describe what (if any) antibiotic resistance has had on your practice.
9. Describe what (if any) antibiotic resistance has had on your community.
10. What do you think would be the most useful strategies to help decreases antibiotic use?

Tools and Technology

1. All clinicians: How do you determine a patient's antibiotic use status?

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a. What resources or tools do you use to decide which antibiotic is most appropriate for a patient?

2. Physicians and maybe pharmacists:
    a. How does the lab impact your antibiotic prescribing?
3. Lab staff: What changes could be made to your lab that would help you to more effectively support antibiotic prescribing/stewardship at your hospital?

Environment

What posters, signs, or other visual cues promoting good antibiotic prescribing are present in your hospital? Where are they located? Which ones do you notice most?

Final: Is there anything I haven't asked you about antibiotic stewardship that you think is important for me to know?

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Reporting checklist for qualitative study.

Based on the SRQR guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SRQR reporting guidelines, and cite them as:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. Acad Med. 2014;89(9):1245-1251.

		Reporting Item	Page Number
	#1	Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended	5
	#2	Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions	2
Problem formulation	#3	Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	3
Purpose or research question	#4	Purpose of the study and specific objectives or questions	2
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research) and guiding theory if appropriate; identifying the	5

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		research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	
Researcher characteristics and reflexivity	#6	Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability	n/a. The team did not feel any characteristics dramatically influenced our devising of the interview guide or the data collection.
Context	#7	Setting / site and salient contextual factors; rationale	4
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	5
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	6
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	5
Data collection	#11	Description of instruments (e.g. interview guides,	Appendix 1

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instruments and technologies		questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	
Units of study	#12	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	5
Data processing	#13	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	6
Data analysis	#14	Process by which inferences, themes, etc. were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	6
Techniques to enhance trustworthiness	#15	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	6
Syntheses and interpretation	#16	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	6
Links to empirical data	#17	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	18-22
Intergration with prior work, implications, transferability and contribution(s) to the field	#18	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	12
Limitations	#19	Trustworthiness and limitations of findings	12
Conflicts of interest	#20	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	1
Funding	#21	Sources of funding and other support; role of funders	1

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in data collection, interpretation and reporting

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Evaluating Antibiotic Stewardship by Interviewing Tertiary Care Hospital Staff in Kerala, India

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Abstract

Objectives: To determine what barriers and facilitators to antibiotic stewardship exist within a healthcare facility.

Setting: 1300 bed tertiary care private hospital located in the state of Kerala, India.

Participants: 31 semi-structured interviews and 4 focus groups with hospital staff ranging from physicians, nurses, pharmacists, and a clinical microbiologist.

Results: Key facilitators of antibiotic stewardship (AS) at the hospital included a dedicated committee overseeing appropriate inpatient antibiotic use, a prompt microbiology lab, a high level of AS understanding among staff, established guidelines for empiric prescribing, and an easily-accessible antibiogram. We identified the following barriers: limited access to clinical pharmacists, physician immunity to change regarding stewardship policies, infrequent antibiotic de-escalation, high physician workload, an incomplete electronic medical record (EMR), inadequate antibiotic stewardship program (ASP) physical visibility, and high antibiotic use in the community.

Conclusions: Opportunities for improvement at this institution include increasing accessibility to clinical pharmacists, implementing strategies to overcome physician immunity to change, and establishing a more accessible and complete EMR. Our findings are likely to be of use to institutions developing ASPs in lower resource settings.

Keywords: Antibiotic stewardship, antibiotic stewardship programs, antibiotic resistance, India, SEIPS

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Strengths and limitations of this study

- Our study is the first of its kind to systematically examine the key barriers and facilitators of implementing an ASP in a low/middle-income country (LMIC).
- We interviewed a variety of healthcare workers: physicians, nurses, clinical pharmacists, and a microbiologist.
- This was a single center study. Thus, transferability of our findings to more resource-limited rural hospitals within India or to other LMIC may not be possible.
- We did not conduct direct observations of practice to correlate with self-reporting.

Background

The United Nations declared antimicrobial resistance to be "the greatest and most urgent global risk" in 2016[1]. Antibiotic overuse and misuse drives antimicrobial resistance[2]. In India, rates of infections caused by antibiotic resistant bacteria are high and increasing[3-11]. Given that the main driver of antibiotic resistance is antibiotic use and misuse, antibiotic stewardship (AS) and antibiotic stewardship programs (ASP) have a critical role in promoting judicious antibiotic use[12].

In a recent review of AS studies spanning every continent, Davey et al. found ASPs were effective in decreasing treatment duration and increasing adherence to antibiotic use policy[13]. While the evidence for ASP effectiveness is growing, there is considerable variation among ASPs in size, activities, and scope. Newly published consensus of an ASP core elements checklist includes experts from twelve countries on six continents and should be considered by healthcare centers when considering their individual ASP, no matter their economic status[14]. This checklist includes some of the elements we identified as areas of strength in this institution: senior hospital management support, a formal ASP, and timely access to laboratory results. Still, we recognize low and middle income countries

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(LMIC) face ASP implementation challenges including limited diagnostic lab capability, inadequate awareness, limited access to quality antibiotics, and high patient census[15]. To date, few studies have explored the challenges facilities in India face carrying out ASPs, such as less available manpower and money dedicated to maintaining a detailed electronic medical record (EMR) compared to higher income country counterparts[16-18]. EMR systems have been found to be one of the most effective ways of keeping records on patient care and allow for easier discussion and feedback on antibiotic choices[17]. We selected India because, as mentioned, antibiotic resistance rates are high and increasing, and our study facility had recently implemented an ASP to address this issue. Thus, we undertook a prospective qualitative study in Kerala, India to examine the barriers and facilitators to practicing AS in a LMIC healthcare setting and to identify opportunities to improve AS.

Methods

Location

In January 2018, we conducted a qualitative study to understand the barriers and facilitators to AS at a 1300 bed tertiary care private hospital located in the state of Kerala, India. This urban hospital, which includes 275 intensive care beds, provides free or subsidized advanced care for two-thirds of its patient population. AS activities began in 2015. The hospital's ASP, members of which include internists, surgeons, a microbiologist, critical care physicians, infection control nurses, and an administrator, began in 2016. The Chief Medical Officer, the head of both the institution as a whole and the ASP itself, initiated the antibiotic stewardship meetings, infectious disease rounds, chart review of patients. Committee members are a mix of junior, mid-level, and senior staff and serve for at least two years with the option to continue involvement afterward.

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Study population

Physicians, nurses, clinical pharmacists, and a microbiologist were identified by the on-site study team by emailing information to staff regarding the project and subsequently approached staff in-person to identify interested participants. We included senior faculty and healthcare professionals working on the critical care medicine and infectious disease teams for interview. Exclusion criteria included non-English speaking staff and staff who were subordinates to any member of the study team.

Data collection

We conducted 31 semi-structured interviews and 4 focus groups with hospital staff involved in AS. Interview guides were developed based on the Systems Engineering Initiative for Patient Safety (SEIPS) framework. This framework evaluates the interactions between the people, organization, tasks, tools/technology, and environment of a given work system, allowing for identification of key areas for improvement or intervention[19]. Interviews were conducted in private rooms at the hospital, and were audio recorded after obtaining verbal consent from the participant. No personal information was recorded, and each interview lasted between 10 and 30 minutes. The interview guides used have been included for reference (Appendix A).

Analysis

All interviews were transcribed and analyzed deductively using the SEIPS framework. One member from the study team manually coded the interview transcripts. Quotations from transcribed interviews were sorted into the SEIPS categories of person, organization, tasks, tools/technology, and physical environment. After all study team members agreed on the identified themes from the interviews, the most prominent

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barriers and facilitators to AS were identified in each category based on number of participant responses. We used the Standards for Reporting Qualitative Research (SRQR) guidelines[20].

Ethics approval

The Institutional Review Board at the University of Wisconsin-Madison granted this study exemption from full review. The Internal Ethics Committee at the participating hospital reviewed the study and granted approval (IRB# 2017-1268).

Patient and Public Involvement statement

The development of our study was informed by many patients' preference to get antibiotics right away, just in case these drugs help. This can influence how healthcare providers deal with prescribing. We did not involve patients with the design or conduct of the study. Results will be disseminated to the involved healthcare workers at staff meetings and electronic communications.

Results

In total, we interviewed 45 hospital faculty and staff. Participants included individual interviews with physicians (27), clinical pharmacists (3), and one microbiologist. We also conducted four focus groups consisting of ASP team members, pharmacists (two groups), and infection control nurses with two to five participants each.

Organization

The hospital's ASP is the key organizational component of promoting judicious antibiotic use and is in addition to the three clinical pharmacists and one infection control nurse the hospital uses as dedicated, full-time stewardship positions. The ASP team evaluates the list of inpatients receiving antibiotics to evaluate "The Five R's" of antibiotic

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prescribing: right drug, right dose, right frequency, right duration, and right indication. When the team identifies opportunities for antibiotic de-escalation or reduced duration, a clinical pharmacist member contacts the prescribing physician to issue treatment recommendations, and the prescribing physician decides whether to modify treatment. Typically the hospital sees 30 "higher antibiotic" prescriptions a day; these are the cases the ASP reviews. Usually the committee has suggestions for five or six cases, most often communicating these with staff via email for recording/tracking purposes. In-person communication during rounds, telephone calls, and text messages to the microbiologists in the lab are also utilized as they are more effective methods of quick communication.

According to about half of respondents, hospital administrative leadership champions the ASP by being involved in the meetings, handling difficult conversations with physicians, and instilling confidence in all staff that the ASP is working with them to improve patient care. Staff in turn view their institution's ASP as a key facilitator of AS at the hospital (Table 1, quotes 1-3). In addition to the ASP itself, 17 interviewees regarded the microbiology lab as a key facilitator of AS. Staff praised the 24-hour lab's promptness and the rapidity with which lab staff uploaded results into the EMR. In addition, many physicians relied on the microbiologist's expertise for help identifying microorganisms in complicated infections (Table 1, quotes 4 and 5). As one physician said, "If we are thinking about a gram positive illness and we get a culture that's gram negative, which is grown very quickly, we totally change our report."

Despite having an effective stewardship program and lab, 16 interviewees identified limited clinical pharmacist availability as a barrier to AS. In India, clinical pharmacists must complete a six year Doctorate program from an accredited university to receive licensure,

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and many physicians recognized clinical pharmacists' knowledge as a critical component of patient care. However, several departments had one clinical pharmacist and many had none at all. Staff worried this lack of pharmacist access may cause clinicians to miss drug interactions or prescribe antibiotics at incorrect dosages (Table 1, quotes 6-8).

Person

During our interviews, staff identified AS activities, such as using the correct antibiotic at the correct dose, as a key component of reducing antibiotic resistance. In addition, staff mentioned they often heard about AS at work. This high level of awareness among staff facilitates AS practices (Table 1, quotes 9-11).

While most interviewed staff demonstrated AS policy understanding, they revealed many physicians resisted accepting suggestions from the ASP. Moreover, several physicians and pharmacists worried other physicians did not acknowledge pharmacists' contributions to patient care. According to nine interviewees, this immunity to change may impede AS practices and contribute to antibiotic resistance through incorrect antibiotic dosing and duration (Table 1, quotes 12 and 13). One clinician described this phenomena for us by saying, "I think clinicians are empowered to think that they know best. They need to recognize the roles of the microbiologists and the pharmacists and should not feel low that they have asked for help." A nurse we spoke to distilled the issue; "Challenges come from navigating human behavior."

Tasks

Staff in 12 interviews felt that clinicians follow established guidelines when prescribing antibiotics when the cause of illness is not yet known. Following a clinical evaluation, the physician orders a culture and initiates a broad-spectrum antibiotic.

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Physicians then use this culture result to modify the original antibiotic used. This process, often called de-escalation, involves selecting an antibiotic which has a more specific spectrum or stopping antibiotic treatment if the cultures do not identify a bacterial infection (Table 1, quote 14).

As a tertiary care facility, this hospital frequently treats high-risk patients who have acquired resistant infections in the community or at other hospitals. Therefore, physicians at our study institution often feel compelled to empirically prescribe broad-spectrum antibiotics while awaiting culture results. However, physicians often forget or refuse to de-escalate antibiotic use due to workload or fear of losing the patient. In our study, physicians and pharmacists in eight interviews worried this lack of de-escalation may increase the risk of antibiotic resistant infections (Table 1, quote 15) and cited de-escalation as the most important issue regarding antibiotic prescribing. Similarly, nine interviewed staff members feared their high workloads may negatively impact their ability to always judiciously prescribe antibiotics. Physicians noted they are often unable to spend sufficient time evaluating a patient and this, along with uncertainty over what exact drugs the patient has already taken pre-admission, leads to antibiotic over-prescription (Table 1, quotes 16 and 17). This happens because if a patient has already taken a certain class of antibiotic and they haven't worked, prescribing more is not going to help.

Tools/Technology

The hospital microbiologist and clinical pharmacists update the hospital antibiogram annually. The antibiogram, which gives the percent of pathogens susceptible to various antimicrobial agents, is accessible on the hospital intranet and divided into Gram positive, Gram negative, and yeast. In 17 interviews, staff members identified this user-

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friendly tool as a key facilitator in selecting antibiotics based on hospital resistance patterns, a critical component of AS (Table 1, quote 18).

In addition to the antibiogram, this hospital also utilizes an EMR, which to save money is built and maintained by the hospital's Information Technology department. The EMR is used to store information on inpatients, a useful addition for identifying immediate drug interactions and thereby reducing harm. However, the EMR does not contain a patient's full scope of antibiotic use, including antibiotic history, duration, and dose. This incompleteness often forces physicians and pharmacists to refer to a patient's paper health record, which one pharmacist described as a "tedious" process (Table 1, quote 19). Moreover, physician workflow does not include entering antibiotic data into the EMR. Due to high work volume, physicians depend on the ward secretary, nursing assistants, or research assistants to update the EMR. As one physician explained, "I see 80 patients a day. So it's not possible for me to spend so much time logging in, recording all this. I don't think it's possible unless I had someone sitting next to me doing just that." (Table 1, quote 20). A dozen interviewed staff members identified this inability to quickly access the full scope of a patient's antibiotic history as a barrier to judiciously prescribing antibiotics.

Environment

Despite having a highly engaged AS team, staff mentioned the hospital did not have signs or posters to increase stewardship awareness, which several staff identified as a potentially useful addition. A few interviewees thought AS policies were sometimes printed and posted but did not "stand out." These printed antibiotic prescribing protocols were not visible to all staff, and 23 interviewed staff members mentioned this limited visibility may inhibit widespread AS awareness. (Table 1, quotes 21 and 22)

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In addition, staff identified high local antibiotic use as a barrier to stewardship. As patients can purchase antibiotics over the counter or have been recently hospitalized at another facility, many patients enter the hospital already using antibiotics. These high use rates often lead to antibiotic resistant infections in the community, forcing physicians to prescribe broad-spectrum antibiotics. Furthermore, several staff feared the impact of high antibiotic use in animal husbandry and fisheries on spreading resistance. Seven staff members wished for enhanced antibiotic prescribing regulations and more AS awareness in greater India (Table 1, quote 23).

Discussion

Our study is the first of its kind in the English language to systematically examine key barriers and facilitators of implementing ASP in a LMIC tertiary hospital. Using the SEIPS model, we examined the implementation of an ASP at a large tertiary care hospital in order to identify opportunities to improve this program.

We found that limited access to clinical pharmacists, physician immunity to change resulting in infrequent antibiotic de-escalation, high physician workload, an inadequate EMR, inadequate physical visibility of stewardship activities, and high antibiotic use in the community were major barriers to effective ASP implementation. The presence of a prompt microbiology laboratory, high level of understanding of AS among staff, easily accessible antibiogram, and established guidelines for empiric prescribing were identified as important facilitators of an effective ASP in this hospital. As Ravi et al. (2017) discovered, we found committed leadership from the administrator was a major factor as well[17].

Our study found limited access to pharmacists was a barrier for an effective ASP. Multidisciplinary rounds with guideline-based antibiotic recommendations for specific

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infections have been found to decrease use and duration of both broad spectrum and high-end, reserve antibiotics[21]. Clinical pharmacists can provide real-time decision support which could significantly improve rates of antibiotic tailoring to culture data[22]. Empowering clinical pharmacists to identify highly misused antibiotics, design guideline-based de-escalation protocols, and participate in multidisciplinary rounds may improve the quality of ASP.

Physician resistance to changes in antibiotic use practices was identified as a barrier to an effective ASP. Factors which influence physician antibiotic prescribing habits include anxiety about missing an infection and the antibiotic prescribing behavior of peers[23]. This is an important active area of research; interventions such as encouraging reflection on practice, the use of audit and feedback, small-group learning with discussions and engagement by senior clinicians, and deploying multidisciplinary teams including clinical pharmacists have been shown to improve prescriber behavior[24,25]. In LMIC settings, we recommend leadership should actively promote ASP activities and their value. Feedback on antibiotic usage and patterns should be disseminated to improve adherence to local or national guidelines at this facility.

We found that the usability and accessibility of the EMR were another barrier to an effective ASP. Adoption of an EMR can improve ASP by providing a centralized location for microbiology results and other relevant clinical data[26]. However, the expense of acquiring and optimizing an EMR system to harness its full potential makes this intervention difficult to implement, particularly in LMIC settings[27].

Our study identified high and indiscriminate community-based antibiotic use as one reason why AS is such a challenge at our study site. Variably-enforced regulations on

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antibiotic dispensing and the availability of antibiotics without a prescription is a widespread problem in many countries, including India[28]. The broad and unregulated use of antibiotics in animal feed and fisheries compounds this barrier[29]. ASP in healthcare settings can be complemented by AS in the community for all uses of antibiotics, with an inclusive "One Health" approach to addressing resistance[30]. While not mentioned by any staff, extensive pollution from pharmaceutical production has also been noted as a driver of resistant bacteria, and this too should be addressed in a One Health approach[31]. The state which our study institution exists, Kerala, is currently the only state in India to have an antibiotic policy. Efforts for federal antibiotic use regulations have some support, but nothing has yet come to fruition.

Our study has limitations. First, this was a single center study. Thus, transferability of our findings to more resource-limited rural hospitals within India or to other LMIC may not be possible. Second, we did not conduct direct observations of practice to correlate with self-reporting. Future studies may identify additional barriers and facilitators by implementing direct observation approaches to collect data on stewardship practices. We also asked staff members if they would like to be interviewed, thus introducing the possibility only those who were really invested in AS would agree.

Conclusion

The use of the SEIPS model to analyze an ASP in an LMIC identified barriers and facilitators within the healthcare work system. Opportunities for improvement at this institution include increasing accessibility to clinical pharmacists, implementing strategies to overcome physician immunity to change, and establishing a more accessible and

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complete EMR. Interventions which account for and address barriers and strengthen facilitators should be tested in future studies for their effect on antimicrobial usage and resistance.

Author Statement

KB created the interview guides, conducted in-person interviews, and wrote, edited, and prepared the manuscript. CS created the interview guides, conducted in-person interviews, and wrote/edited the manuscript. JK edited the manuscript. LK conducted on-site data collection and wrote/edited the manuscript. MVJ assisted with on-site data collection and edited the manuscript. SS devised the project and edited the manuscript. NS obtained funding, devised the project, and edited the manuscript. AS assisted with the grant and edited the manuscript. DS assisted with the grant and wrote/edited the manuscript.

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Table 1. Themes identified from SEIPS components with corresponding representative quotations

Theme	Representative Quote
Organization	
Antimicrobial Stewardship Program	1. "We audit to make sure the right indication is happening. We check to see the dosage is correct and monitor what's happening here to track our prescriptions." (pharmacist)
	2. "Every year we do something with the antibiotic prescription program. Along with infection control. Usually a three-day program for doctors and one day is dedicated to antibiotic stewardship. Speakers from all over the country [come] and we take about 30-35 doctors a year and try to teach them about antibiotic stewardship." (infection control nurse)
	3. “The medical superintendent is a part of our team. I don’t think you can get much higher up than that. The management is very supportive.” (pharmacist)
Microbiology laboratory	4. "Our microbiology lab is one of the best in the country. They are very reliable and help us immensely." (physician)
	5. “Whenever the lab grows something in the culture, could be six hours, ten hours, we are called and told. So that does impact our management. If we are thinking about a gram positive illness and we get a culture that’s gram negative, which is grown very quickly, we totally change our report. We are informed pretty quickly.” (physician)

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Clinical pharmacist availability	6. "[Pharmacists are] not routinely in the ICU. I wish more pharmacists would tell physicians their doses or their drug interactions are wrong, but I don't see them in the cardiac or pediatric ICU." (physician)
	7. "We have one pharmacist in our ICU, she visits. The problem with her is she's overworked. She's alone. She comes on the rounds only sometimes and comes around and checks the antibiotics dosing is correct. But duration and all others are decided by physicians. If there were more of them it would be much better." (physician)
	8. "If a clinician is working alone, we may not have much concern about things that pharmacists are more aware of, like drug interactions. Routine medications may have interactions also, so pharmacists' help is needed. That type of information is more with the pharmacists, not the clinicians. They are not always available." (physician)
Person	
Antibiotic stewardship knowledge	9. "Antibiotic stewardship is a standardized practice with the right treatment at the right time." (physician)
	10. "To me antibiotic stewardship is to start judicious antibiotics…I won't say to start low antibiotics, I say to start optimum antibiotics." (physician)
	11. "Most of us here are aware of these ideas. For us, it's about everything that has to do with a prescription. The ultimate aim is judicious use of antibiotics. We need to use the right antibiotics, the right dose." (physician)

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Physician resistance to antibiotic stewardship policies	12. "I think clinicians are empowered to think that they know best. They need to recognize the roles of the microbiologists and the pharmacists and should not feel low that they have asked for help." (physician)
	13. "Challenges come from navigating human behavior. Sometimes you'll recommend things but people just won't listen to you." (infection control nurse)
Tasks	
Antibiotic prescribing	14. "We have a high patient load and socioeconomic status is a big deal. Poverty and malnourished children are a reality. We can't wait for cultures. We have protocols to start them on antibiotics according to which ones have been most successful here." (physician)
	15. "I think it's a problem all over India, because the first antibiotics they prescribe is the carbapenems. And once they prescribe it is never de-escalated or rarely de-escalated. Basically they go, 'let's continue. What the culture says? I don't want to do that. Let's just continue because he's improving.' So it's a major, major, major problem." (physician)
Workload	16. "Sometimes we are busy and we forget pre admission drugs which are missed because we are more worried about the current problems, and there are so many the patient is already on, that we need to continue." (physician)
	17. "Our work here does affect how long you can spend on individual cases." (infection control nurse)

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Tools and Technology	
Antibiogram	18. "It is an annual antibiogram. We divide it into gram positive, gram negative, and yeast. We also have a blood gram positive from blood isolates, negative, and yeast. They are separate. We follow international guidelines so for any isolate that is more than 30, we take them and follow the rules. Every year it is updated. This year they are trying to involve more pharmacists" (infection control nurse)
Electronic medical record	19. "If I look today at the record, I can only see what they took today. The current medications only. Not what they got yesterday. I can't trace the meropenem. To see all the drugs we have to go to the paper medical record room. It's a very tedious process. We don't know the dose or duration or all the drugs…if the patient returns in a few weeks, we don't know what they were taking and what will be effective." (pharmacist)
	20. "I see 80 patients a day. So it's not possible for me to spend so much time logging in, recording all this. I don't think it's possible unless I had someone sitting next to me doing just that." (physician)
Environment	
Posters or signs promoting antibiotic stewardship awareness	21. "It's only in protocols, which we do print out only for doctors. Nurses don't see that." (physician)
	22. "We have some print-outs on our notice board about colistin and other higher-end antibiotics…but we don't have posters. As for the printouts, they aren't that catchy." (physician)

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High levels of community antibiotic use	23. "Outside the hospital this is a rampant problem in India. There is much abuse and misuse of antibiotics. Anyone can just go to a roadside pharmacy and describe their symptoms and get antibiotics over the counter just like that. They just go to the guy sitting there and get whatever. I think we should make it much harder to get antibiotics." (physician)

Frequently used abbreviations:

LMIC: low and middle income countries

ASP: antibiotic stewardship program

AS: antibiotic stewardship

SEIPS: Systems Engineering Initiative for Patient Safety

EMR: electronic medical record

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Appendix A: Antibiotic Stewardship Interview Questions

Interviewer: Antibiotic stewardship refers to the judicious use of antibiotics, and is a critical component of reducing antibiotic resistance. Components of antibiotic stewardship involve drug expertise, evaluating ongoing antibiotic treatment, monitoring prescribing practices, and reporting information on antibiotic use and resistance.

Your responses will be recorded with a voice recorder and transcribed, but the responses will be de-identified in any data set and your identity will be kept confidential.

Person

1. How do you define antibiotic stewardship?
2. What do you think of antibiotic stewardship as an infectious disease prevention strategy?
3. Describe your level of interaction working with infectious disease specialists at your hospital.
4. Physician/Nurse
    a. Describe your work with pharmacists in your hospital.
        i. If poor availability/they don't work with pharmacists: What factors limit their availability to you?
        ii. How do you work with pharmacists on specific patients?
        iii. In an ideal situation, what would be different about how you work with the pharmacists?
    b. Tell me about your workload.
        i. How does your workload impact your ability to complete your job responsibilities?
5. All clinicians: Describe employee turnover on your ward

Organization

1. Describe your experience regarding antimicrobial stewardship education in your facility.
    a. What is your view of these trainings (how likely are you to attend? Do you apply the information to your practice? Who attends?)?
2. What do you hear about antimicrobial stewardship at work?
3. Describe a time a new policy was implemented on your ward/in your lab.
    a. What challenges were encountered? What went well? How did this compare to other times when new policies were implemented?
    b. How were staff involved in the development of the new policy? How are they typically involved in policy development
4. Tell me about your interactions with people involved in the antibiotic stewardship program.
    a. What types of things do you collaborate on/communicate about?
    b. How could your interactions be improved?
5. What is your sense of how hospital leaders/management are involved in antibiotic stewardship efforts in your ward/lab?

6. All clinicians: How could antibiotic prescribing be improved in your facility? Tell me about empiric prescribing at your hospital. What factors should be considered when prescribing an antibiotic if the cause of illness is not yet known?

Tasks

1. Lab Staff
    a. Describe how you create an antibiogram.
        i. How does creating an antibiogram fit in with your other job responsibilities?
        ii. How often do you update the antibiogram?
        iii. What is the scope of the antibiogram?
2. Nurses
    a. What antibiotic stewardship practices are you responsible for on your ward?
    b. How often do you review medications? Describe your review process.
    c. What do you do when antibiotic usage seems questionable? Do you or your team decide together?
    d. Are routine audits of antibiotic use conducted on your ward?
3. Pharmacists
    a. What is your process when an antibiotic is ordered?
        i. What are your selection review practices? Describe your collaboration with physicians.
        ii. Describe your antibiogram use, including successes and challenges. How frequently is it updated?
4. Physicians
    a. Describe your antibiotic selection process, including any guidelines you may use in making your decision.
        i. Describe your antibiogram use, including successes and challenges. How frequently is it updated?
        ii. How often are those guidelines adhered to in your workplace? If infrequently, what are the barriers to adherence?
    b. Describe your review of antibiotic selection, including after the drug has been prescribed and after you have obtained culture results.
5. All clinicians: Where do you store information on antibiotic use (dosage, duration, indication)?
6. All clinicians: How often/how many cases of treatment failure related to resistance have you seen?
7. All staff: Evaluate the effect of your workload on your ability to implement antibiotic stewardship activities.
8. Describe what (if any) antibiotic resistance has had on your practice.
9. Describe what (if any) antibiotic resistance has had on your community.
10. What do you think would be the most useful strategies to help decreases antibiotic use?

Tools and Technology

1. All clinicians: How do you determine a patient's antibiotic use status?

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a. What resources or tools do you use to decide which antibiotic is most appropriate for a patient?

2. Physicians and maybe pharmacists:
   a. How does the lab impact your antibiotic prescribing?
3. Lab staff: What changes could be made to your lab that would help you to more effectively support antibiotic prescribing/stewardship at your hospital?

Environment

What posters, signs, or other visual cues promoting good antibiotic prescribing are present in your hospital? Where are they located? Which ones do you notice most?

Final: Is there anything I haven't asked you about antibiotic stewardship that you think is important for me to know?

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Reporting checklist for qualitative study.

Based on the SRQR guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SRQR reporting guidelines, and cite them as:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. Acad Med. 2014;89(9):1245-1251.

		Reporting Item	Page Number
	#1	Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended	5
	#2	Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions	2
Problem formulation	#3	Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	3
Purpose or research question	#4	Purpose of the study and specific objectives or questions	2
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research) and guiding theory if appropriate; identifying the	5

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		research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	
Researcher characteristics and reflexivity	#6	Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability	n/a. The team did not feel any characteristics dramatically influenced our devising of the interview guide or the data collection.
Context	#7	Setting / site and salient contextual factors; rationale	4
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	5
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	6
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	5
Data collection	#11	Description of instruments (e.g. interview guides,	Appendix 1

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instruments and technologies		questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	
Units of study	#12	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	5
Data processing	#13	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	6
Data analysis	#14	Process by which inferences, themes, etc. were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	6
Techniques to enhance trustworthiness	#15	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	6
Syntheses and interpretation	#16	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	6
Links to empirical data	#17	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	18-22
Intergration with prior work, implications, transferability and contribution(s) to the field	#18	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	12
Limitations	#19	Trustworthiness and limitations of findings	12
Conflicts of interest	#20	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	1
Funding	#21	Sources of funding and other support; role of funders	1

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in data collection, interpretation and reporting

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Manuscripts

Evaluating Antibiotic Stewardship by Interviewing Tertiary Care Hospital Staff in Kerala, India

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writing and editing the manuscript. AS helped with the grant and edited the manuscript. JK edited the manuscript.

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Abstract

Objectives: To determine what barriers and facilitators to antibiotic stewardship exist within a healthcare facility.

Setting: 1300 bed tertiary care private hospital located in the state of Kerala, India.

Participants: 31 semi-structured interviews and 4 focus groups with hospital staff ranging from physicians, nurses, pharmacists, and a clinical microbiologist.

Results: Key facilitators of antibiotic stewardship (AS) at the hospital included a dedicated committee overseeing appropriate inpatient antibiotic use, a prompt microbiology lab, a high level of AS understanding among staff, established guidelines for empiric prescribing, and an easily-accessible antibiogram. We identified the following barriers: limited access to clinical pharmacists, physician immunity to change regarding stewardship policies, infrequent antibiotic de-escalation, high physician workload, an incomplete electronic medical record (EMR), inadequate antibiotic stewardship program (ASP) physical visibility, and high antibiotic use in the community.

Conclusions: Opportunities for improvement at this institution include increasing accessibility to clinical pharmacists, implementing strategies to overcome physician immunity to change, and establishing a more accessible and complete EMR. Our findings are likely to be of use to institutions developing ASPs in lower resource settings.

Keywords: Antibiotic stewardship, antibiotic stewardship programs, antibiotic resistance, India, SEIPS

Strengths and limitations of this study

- Our study is the first of its kind to systematically examine the key barriers and facilitators of implementing an ASP in a low/middle-income country (LMIC).
- We interviewed a variety of healthcare workers: physicians, nurses, clinical pharmacists, and a microbiologist.
- This was a single center study. Thus, transferability of our findings to more resource-limited rural hospitals within India or to other LMIC may not be possible.
- We did not conduct direct observations of practice to correlate with self-reporting.

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Background

The United Nations declared antimicrobial resistance to be "the greatest and most urgent global risk" in 2016[1]. Antibiotic overuse and misuse drives antimicrobial resistance[2]. In India, rates of infections caused by antibiotic resistant bacteria are high and increasing[3-11]. Given that the main driver of antibiotic resistance is antibiotic use and misuse, antibiotic stewardship (AS) and antibiotic stewardship programs (ASP) have a critical role in promoting judicious antibiotic use[12].

In a recent review of AS studies spanning every continent, Davey et al. found ASPs were effective in decreasing treatment duration and increasing adherence to antibiotic use policy[13]. While the evidence for ASP effectiveness is growing, there is considerable variation among ASPs in size, activities, and scope. Newly published consensus of an ASP core elements checklist includes experts from twelve countries on six continents and should be considered by healthcare centers when considering their individual ASP, no matter their economic status[14]. This checklist includes some of the elements we identified as areas of strength in this institution: senior hospital management support, a formal ASP, and timely access to laboratory results. Still, we recognize low and middle income countries (LMIC) face

ASP implementation challenges including limited diagnostic lab capability, inadequate awareness, limited access to quality antibiotics, and high patient census[15]. To date, few studies have explored the challenges facilities in India face carrying out ASPs, such as less available manpower and money dedicated to maintaining a detailed electronic medical record (EMR) compared to higher income country counterparts[16-18]. EMR systems have been found to be one of the most effective ways of keeping records on patient care and allow for easier discussion and feedback on antibiotic choices[17]. We selected India because, as mentioned, antibiotic resistance rates are high and increasing, and our study facility had recently implemented an ASP to address this issue. Thus, we undertook a prospective qualitative study in Kerala, India to examine the barriers and facilitators to practicing AS in a LMIC healthcare setting and to identify opportunities to improve AS.

Methods

Location

In January 2018, we conducted a qualitative study to understand the barriers and facilitators to AS at a 1300 bed tertiary care private hospital located in the state of Kerala, India. This urban hospital, which includes 275 intensive care beds, provides free or subsidized advanced care for two-thirds of its patient population. AS activities began in 2015. The hospital's ASP, members of which include internists, surgeons, a microbiologist, critical care physicians, infection control nurses, and an administrator, began in 2016. The Chief Medical Officer, the head of both the institution as a whole and the ASP itself, initiated the antibiotic stewardship meetings, infectious disease rounds, chart review of patients. Committee members are a mix of junior, mid-level, and senior staff and serve for at least two years with the option to continue involvement afterward.

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Study population

Physicians, nurses, clinical pharmacists, and a microbiologist were identified by the on-site study team by emailing information to staff regarding the project and subsequently approached staff in-person to identify interested participants. We included senior faculty and healthcare professionals working on the critical care medicine and infectious disease teams for interview. Exclusion criteria included non-English speaking staff and staff who were subordinates to any member of the study team.

Data collection

We conducted 31 semi-structured interviews and 4 focus groups with hospital staff involved in AS. Interview guides were developed based on the Systems Engineering Initiative for Patient Safety (SEIPS) framework. This framework evaluates the interactions between the people, organization, tasks, tools/technology, and environment of a given work system, allowing for identification of key areas for improvement or intervention[19]. Interviews were conducted in private rooms at the hospital, and were audio recorded after obtaining verbal consent from the participant. No personal information was recorded, and each interview lasted between 10 and 30 minutes. The interview guides used have been included for reference (Appendix A).

Analysis

All interviews were transcribed and analyzed deductively using the SEIPS framework. One member from the study team manually coded the interview transcripts. Quotations from transcribed interviews were sorted into the SEIPS categories of person, organization, tasks, tools/technology, and physical environment. After all study team members agreed on the identified themes from the interviews, the most prominent barriers and facilitators to AS

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were identified in each category based on number of participant responses. We used the Standards for Reporting Qualitative Research (SRQR) guidelines[20].

Ethics approval

The Institutional Review Board at the University of Wisconsin-Madison granted this study exemption from full review. The Internal Ethics Committee at the participating hospital reviewed the study and granted approval (IRB# 2017-1268).

Patient and Public Involvement statement

The development of our study was informed by many patients' preference to get antibiotics right away, just in case these drugs help. This can influence how healthcare providers deal with prescribing. We did not involve patients with the design or conduct of the study. Results will be disseminated to the involved healthcare workers at staff meetings and electronic communications.

Results

In total, we interviewed 45 hospital faculty and staff. Participants included individual interviews with physicians (27), clinical pharmacists (3), and one microbiologist. We also conducted four focus groups consisting of ASP team members, pharmacists (two groups), and infection control nurses with two to five participants each.

Organization

The hospital's ASP is the key organizational component of promoting judicious antibiotic use and is in addition to the three clinical pharmacists and one infection control nurse the hospital uses as dedicated, full-time stewardship positions. The ASP team evaluates the list of inpatients receiving antibiotics to evaluate "The Five R's" of antibiotic prescribing: right drug, right dose, right frequency, right duration, and right indication. When

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the team identifies opportunities for antibiotic de-escalation or reduced duration, a clinical pharmacist member contacts the prescribing physician to issue treatment recommendations, and the prescribing physician decides whether to modify treatment. Typically the hospital sees 30 "higher antibiotic" prescriptions a day; these are the cases the ASP reviews. Usually the committee has suggestions for five or six cases, most often communicating these with staff via email for recording/tracking purposes. In-person communication during rounds, telephone calls, and text messages to the microbiologists in the lab are also utilized as they are more effective methods of quick communication.

According to about half of respondents, hospital administrative leadership champions the ASP by being involved in the meetings, handling difficult conversations with physicians, and instilling confidence in all staff that the ASP is working with them to improve patient care. Staff in turn view their institution's ASP as a key facilitator of AS at the hospital (Table 1, quotes 1-3). In addition to the ASP itself, 17 interviewees regarded the microbiology lab as a key facilitator of AS. Staff praised the 24-hour lab's promptness and the rapidity with which lab staff uploaded results into the EMR. In addition, many physicians relied on the microbiologist's expertise for help identifying microorganisms in complicated infections (Table 1, quotes 4 and 5). As one physician said, "If we are thinking about a gram positive illness and we get a culture that's gram negative, which is grown very quickly, we totally change our report."

Despite having an effective stewardship program and lab, 16 interviewees identified limited clinical pharmacist availability as a barrier to AS. In India, clinical pharmacists must complete a six year Doctorate program from an accredited university to receive licensure, and many physicians recognized clinical pharmacists' knowledge as a critical component of

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patient care. However, several departments had one clinical pharmacist and many had none at all. Staff worried this lack of pharmacist access may cause clinicians to miss drug interactions or prescribe antibiotics at incorrect dosages (Table 1, quotes 6-8).

Person

During our interviews, staff identified AS activities, such as using the correct antibiotic at the correct dose, as a key component of reducing antibiotic resistance. In addition, staff mentioned they often heard about AS at work. This high level of awareness among staff facilitates AS practices (Table 1, quotes 9-11).

While most interviewed staff demonstrated AS policy understanding, they revealed many physicians resisted accepting suggestions from the ASP. Moreover, several physicians and pharmacists worried other physicians did not acknowledge pharmacists' contributions to patient care. According to nine interviewees, this immunity to change may impede AS practices and contribute to antibiotic resistance through incorrect antibiotic dosing and duration (Table 1, quotes 12 and 13). One clinician described this phenomena for us by saying, "I think clinicians are empowered to think that they know best. They need to recognize the roles of the microbiologists and the pharmacists and should not feel low that they have asked for help." A nurse we spoke to distilled the issue; "Challenges come from navigating human behavior." Staff immunity to change may present challenges for other LMIC as well; strategies which have been helping this particular facility are publishing easily accessible guidelines and committing to persistent interaction between staff and the ASP. In this way, AS is a priority which is tended to and fostered as an institution-wide value.

Tasks

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Staff in 12 interviews felt that clinicians follow established guidelines when prescribing antibiotics when the cause of illness is not yet known. Following a clinical evaluation, the physician orders a culture and initiates a broad-spectrum antibiotic. Physicians then use this culture result to modify the original antibiotic used. This process, often called de-escalation, involves selecting an antibiotic which has a more specific spectrum or stopping antibiotic treatment if the cultures do not identify a bacterial infection (Table 1, quote 14).

As a tertiary care facility, this hospital frequently treats high-risk patients who have acquired resistant infections in the community or at other hospitals. Therefore, physicians at our study institution often feel compelled to empirically prescribe broad-spectrum antibiotics while awaiting culture results. However, physicians often forget or refuse to de-escalate antibiotic use due to workload or fear of losing the patient. In our study, physicians and pharmacists in eight interviews worried this lack of de-escalation may increase the risk of antibiotic resistant infections (Table 1, quote 15) and cited de-escalation as the most important issue regarding antibiotic prescribing. Similarly, nine interviewed staff members feared their high workloads may negatively impact their ability to always judiciously prescribe antibiotics. Physicians noted they are often unable to spend sufficient time evaluating a patient and this, along with uncertainty over what exact drugs the patient has already taken pre-admission, leads to antibiotic over-prescription (Table 1, quotes 16 and 17). This happens because if a patient has already taken a certain class of antibiotic and they haven't worked, prescribing more is not going to help.

Tools/Technology

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The hospital microbiologist and clinical pharmacists update the hospital antibiogram annually. The antibiogram, which gives the percent of pathogens susceptible to various antimicrobial agents, is accessible on the hospital intranet and divided into Gram positive, Gram negative, and yeast. In 17 interviews, staff members identified this user-friendly tool as a key facilitator in selecting antibiotics based on hospital resistance patterns, a critical component of AS (Table 1, quote 18).

In addition to the antibiogram, this hospital also utilizes an EMR, which to save money is built and maintained by the hospital's Information Technology department. The EMR is used to store information on inpatients, a useful addition for identifying immediate drug interactions and thereby reducing harm. However, the EMR does not contain a patient's full scope of antibiotic use, including antibiotic history, duration, and dose. This incompleteness often forces physicians and pharmacists to refer to a patient's paper health record, which one pharmacist described as a "tedious" process (Table 1, quote 19). Moreover, physician workflow does not include entering antibiotic data into the EMR. Due to high work volume, physicians depend on the ward secretary, nursing assistants, or research assistants to update the EMR. As one physician explained, "I see 80 patients a day. So it's not possible for me to spend so much time logging in, recording all this. I don't think it's possible unless I had someone sitting next to me doing just that." (Table 1, quote 20). A dozen interviewed staff members identified this inability to quickly access the full scope of a patient's antibiotic history as a barrier to judiciously prescribing antibiotics.

Environment

Despite having a highly engaged AS team, staff mentioned the hospital did not have signs or posters to increase stewardship awareness, which several staff identified as a

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potentially useful addition. A few interviewees thought AS policies were sometimes printed and posted but did not "stand out." These printed antibiotic prescribing protocols were not visible to all staff, and 23 interviewed staff members mentioned this limited visibility may inhibit widespread AS awareness. (Table 1, quotes 21 and 22)

In addition, staff identified high local antibiotic use as a barrier to stewardship. As patients can purchase antibiotics over the counter or have been recently hospitalized at another facility, many patients enter the hospital already using antibiotics. These high use rates often lead to antibiotic resistant infections in the community, forcing physicians to prescribe broad-spectrum antibiotics. Furthermore, several staff feared the impact of high antibiotic use in animal husbandry and fisheries on spreading resistance. Seven staff members wished for enhanced antibiotic prescribing regulations and more AS awareness in greater India (Table 1, quote 23).

Discussion

Our study is the first of its kind in the English language to systematically examine key barriers and facilitators of implementing ASP in a LMIC tertiary hospital. Using the SEIPS model, we examined the implementation of an ASP at a large tertiary care hospital in order to identify opportunities to improve this program.

We found that limited access to clinical pharmacists, physician immunity to change resulting in infrequent antibiotic de-escalation, high physician workload, an inadequate EMR, inadequate physical visibility of stewardship activities, and high antibiotic use in the community were major barriers to effective ASP implementation. The presence of a prompt microbiology laboratory, high level of understanding of AS among staff, easily accessible antibiogram, and established guidelines for empiric prescribing were identified as important

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facilitators of an effective ASP in this hospital. As Ravi et al. (2017) discovered, we found committed leadership from the administrator was a major factor as well[17]. This could be a main driver of why AS understanding and opinions about the facility's AS efforts were fairly unified among interviewees regardless of if they were involved in the ASP team or not.

Our study found limited access to pharmacists was a barrier for an effective ASP. Multidisciplinary rounds with guideline-based antibiotic recommendations for specific infections have been found to decrease use and duration of both broad spectrum and high-end, reserve antibiotics[21]. Clinical pharmacists can provide real-time decision support which could significantly improve rates of antibiotic tailoring to culture data[22]. Empowering clinical pharmacists to identify highly misused antibiotics, design guideline-based de-escalation protocols, and participate in multidisciplinary rounds may improve the quality of ASP.

Physician resistance to changes in antibiotic use practices was identified as a barrier to an effective ASP. Factors which influence physician antibiotic prescribing habits include anxiety about missing an infection and the antibiotic prescribing behavior of peers[23]. This is an important active area of research; interventions such as encouraging reflection on practice, the use of audit and feedback, small-group learning with discussions and engagement by senior clinicians, and deploying multidisciplinary teams including clinical pharmacists have been shown to improve prescriber behavior[24,25]. In LMIC settings, we recommend leadership should actively promote ASP activities and their value. Feedback on antibiotic usage and patterns should be disseminated to improve adherence to local or national guidelines at this facility.

We found that the usability and accessibility of the EMR were another barrier to an effective ASP. Adoption of an EMR can improve ASP by providing a centralized location for

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microbiology results and other relevant clinical data[26]. However, the expense of acquiring and optimizing an EMR system to harness its full potential makes this intervention difficult to implement, particularly in LMIC settings[27].

Our study identified high and indiscriminate community-based antibiotic use as one reason why AS is such a challenge at our study site. Variably-enforced regulations on antibiotic dispensing and the availability of antibiotics without a prescription is a widespread problem in many countries, including India[28]. The broad and unregulated use of antibiotics in animal feed and fisheries compounds this barrier[29]. ASP in healthcare settings can be complemented by AS in the community for all uses of antibiotics, with an inclusive "One Health" approach to addressing resistance[30]. While not mentioned by any staff, extensive pollution from pharmaceutical production has also been noted as a driver of resistant bacteria, and this too should be addressed in a One Health approach[31]. The state which our study institution exists, Kerala, is currently the only state in India to have an antibiotic policy. Efforts for federal antibiotic use regulations have some support, but nothing has yet come to fruition.

Our study has limitations. First, this was a single center study. Thus, transferability of our findings to more resource-limited rural hospitals within India or to other LMIC may not be possible. Second, we did not conduct direct observations of practice to correlate with self-reporting. Future studies may identify additional barriers and facilitators by implementing direct observation approaches to collect data on stewardship practices. We also asked staff members if they would like to be interviewed, thus introducing the possibility only those who were really invested in AS would agree.

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Conclusion

The use of the SEIPS model to analyze an ASP in an LMIC identified barriers and facilitators within the healthcare work system. Opportunities for improvement at this institution include increasing accessibility to clinical pharmacists, implementing strategies to overcome physician immunity to change, and establishing a more accessible and complete EMR. Interventions which account for and address barriers and strengthen facilitators should be tested in future studies for their effect on antimicrobial usage and resistance.

Author Statement

KB created the interview guides, conducted in-person interviews, and wrote, edited, and prepared the manuscript. CS created the interview guides, conducted in-person interviews, and wrote/edited the manuscript. JK edited the manuscript. LK conducted on-site data collection and wrote/edited the manuscript. MVJ assisted with on-site data collection and edited the manuscript. SS devised the project and edited the manuscript. NS obtained funding, devised the project, and edited the manuscript. AS assisted with the grant and edited the manuscript. DS assisted with the grant and wrote/edited the manuscript.

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Table 1. Themes identified from SEIPS components with corresponding representative quotations

Theme	Representative Quote
Organization	
Antimicrobial Stewardship Program	1. "We audit to make sure the right indication is happening. We check to see the dosage is correct and monitor what's happening here to track our prescriptions." (pharmacist)
	2. "Every year we do something with the antibiotic prescription program. Along with infection control. Usually a three-day program for doctors and one day is dedicated to antibiotic stewardship. Speakers from all over the country [come] and we take about 30-35 doctors a year and try to teach them about antibiotic stewardship." (infection control nurse)
	3. “The medical superintendent is a part of our team. I don’t think you can get much higher up than that. The management is very supportive.” (pharmacist)
Microbiology laboratory	4. "Our microbiology lab is one of the best in the country. They are very reliable and help us immensely." (physician)

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	5. “Whenever the lab grows something in the culture, could be six hours, ten hours, we are called and told. So that does impact our management. If we are thinking about a gram positive illness and we get a culture that’s gram negative, which is grown very quickly, we totally change our report. We are informed pretty quickly.” (physician)
Clinical pharmacist availability	6. “[Pharmacists are] not routinely in the ICU. I wish more pharmacists would tell physicians their doses or their drug interactions are wrong, but I don’t see them in the cardiac or pediatric ICU.” (physician)
	7. “We have one pharmacist in our ICU, she visits. The problem with her is she’s overworked. She’s alone. She comes on the rounds only sometimes and comes around and checks the antibiotics dosing is correct. But duration and all others are decided by physicians. If there were more of them it would be much better.” (physician)
	8. “If a clinician is working alone, we may not have much concern about things that pharmacists are more aware of, like drug interactions. Routine medications may have interactions also, so pharmacists’ help is needed. That type of information is more with the pharmacists, not the clinicians. They are not always available.” (physician)
Person	
Antibiotic stewardship knowledge	9. “Antibiotic stewardship is a standardized practice with the right treatment at the right time.” (physician)

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	10. “To me antibiotic stewardship is to start judicious antibiotics…I won’t say to start low antibiotics, I say to start optimum antibiotics.” (physician)
	11. “Most of us here are aware of these ideas. For us, it’s about everything that has to do with a prescription. The ultimate aim is judicious use of antibiotics. We need to use the right antibiotics, the right dose.” (physician)
Physician resistance to antibiotic stewardship policies	12. “I think clinicians are empowered to think that they know best. They need to recognize the roles of the microbiologists and the pharmacists and should not feel low that they have asked for help.” (physician)
	13. “Challenges come from navigating human behavior. Sometimes you’ll recommend things but people just won’t listen to you.” (infection control nurse)
Tasks	
Antibiotic prescribing	14. “We have a high patient load and socioeconomic status is a big deal. Poverty and malnourished children are a reality. We can’t wait for cultures. We have protocols to start them on antibiotics according to which ones have been most successful here.” (physician)
	15. “I think it’s a problem all over India, because the first antibiotics they prescribe is the carbapenems. And once they prescribe it is never de-escalated or rarely de-escalated. Basically they go, ‘let’s continue. What the culture says? I don’t want to do that. Let’s just continue because he’s improving.’ So it’s a major, major, major problem.” (physician)

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Workload	16. "Sometimes we are busy and we forget pre admission drugs which are missed because we are more worried about the current problems, and there are so many the patient is already on, that we need to continue." (physician)
	17. "Our work here does affect how long you can spend on individual cases." (infection control nurse)
Tools and Technology	
Antibiogram	18. "It is an annual antibiogram. We divide it into gram positive, gram negative, and yeast. We also have a blood gram positive from blood isolates, negative, and yeast. They are separate. We follow international guidelines so for any isolate that is more than 30, we take them and follow the rules. Every year it is updated. This year they are trying to involve more pharmacists" (infection control nurse)
Electronic medical record	19. "If I look today at the record, I can only see what they took today. The current medications only. Not what they got yesterday. I can't trace the meropenem. To see all the drugs we have to go to the paper medical record room. It's a very tedious process. We don't know the dose or duration or all the drugs…if the patient returns in a few weeks, we don't know what they were taking and what will be effective." (pharmacist)
	20. "I see 80 patients a day. So it's not possible for me to spend so much time logging in, recording all this. I don't think it's possible unless I had someone sitting next to me doing just that." (physician)

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Environment	
Posters or signs promoting antibiotic stewardship awareness	21. "It's only in protocols, which we do print out only for doctors. Nurses don't see that." (physician)
	22. "We have some print-outs on our notice board about colistin and other higher-end antibiotics…but we don't have posters. As for the printouts, they aren't that catchy." (physician)
High levels of community antibiotic use	23. "Outside the hospital this is a rampant problem in India. There is much abuse and misuse of antibiotics. Anyone can just go to a roadside pharmacy and describe their symptoms and get antibiotics over the counter just like that. They just go to the guy sitting there and get whatever. I think we should make it much harder to get antibiotics." (physician)

Frequently used abbreviations:

LMIC: low and middle income countries

ASP: antibiotic stewardship program

AS: antibiotic stewardship

SEIPS: Systems Engineering Initiative for Patient Safety

EMR: electronic medical record

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Appendix A: Antibiotic Stewardship Interview Questions

Interviewer: Antibiotic stewardship refers to the judicious use of antibiotics, and is a critical component of reducing antibiotic resistance. Components of antibiotic stewardship involve drug expertise, evaluating ongoing antibiotic treatment, monitoring prescribing practices, and reporting information on antibiotic use and resistance.

Your responses will be recorded with a voice recorder and transcribed, but the responses will be de-identified in any data set and your identity will be kept confidential.

Person

1. How do you define antibiotic stewardship?
2. What do you think of antibiotic stewardship as an infectious disease prevention strategy?
3. Describe your level of interaction working with infectious disease specialists at your hospital.
4. Physician/Nurse
    a. Describe your work with pharmacists in your hospital.
        i. If poor availability/they don't work with pharmacists: What factors limit their availability to you?
        ii. How do you work with pharmacists on specific patients?
        iii. In an ideal situation, what would be different about how you work with the pharmacists?
    b. Tell me about your workload.
        i. How does your workload impact your ability to complete your job responsibilities?
5. All clinicians: Describe employee turnover on your ward

Organization

1. Describe your experience regarding antimicrobial stewardship education in your facility.
    a. What is your view of these trainings (how likely are you to attend? Do you apply the information to your practice? Who attends?)?
2. What do you hear about antimicrobial stewardship at work?
3. Describe a time a new policy was implemented on your ward/in your lab.
    a. What challenges were encountered? What went well? How did this compare to other times when new policies were implemented?
    b. How were staff involved in the development of the new policy? How are they typically involved in policy development
4. Tell me about your interactions with people involved in the antibiotic stewardship program.
    a. What types of things do you collaborate on/communicate about?
    b. How could your interactions be improved?
5. What is your sense of how hospital leaders/management are involved in antibiotic stewardship efforts in your ward/lab?

6. All clinicians: How could antibiotic prescribing be improved in your facility? Tell me about empiric prescribing at your hospital. What factors should be considered when prescribing an antibiotic if the cause of illness is not yet known?

Tasks

1. Lab Staff
    a. Describe how you create an antibiogram.
        i. How does creating an antibiogram fit in with your other job responsibilities?
        ii. How often do you update the antibiogram?
        iii. What is the scope of the antibiogram?
2. Nurses
    a. What antibiotic stewardship practices are you responsible for on your ward?
    b. How often do you review medications? Describe your review process.
    c. What do you do when antibiotic usage seems questionable? Do you or your team decide together?
    d. Are routine audits of antibiotic use conducted on your ward?
3. Pharmacists
    a. What is your process when an antibiotic is ordered?
        i. What are your selection review practices? Describe your collaboration with physicians.
        ii. Describe your antibiogram use, including successes and challenges. How frequently is it updated?
4. Physicians
    a. Describe your antibiotic selection process, including any guidelines you may use in making your decision.
        i. Describe your antibiogram use, including successes and challenges. How frequently is it updated?
        ii. How often are those guidelines adhered to in your workplace? If infrequently, what are the barriers to adherence?
    b. Describe your review of antibiotic selection, including after the drug has been prescribed and after you have obtained culture results.
5. All clinicians: Where do you store information on antibiotic use (dosage, duration, indication)?
6. All clinicians: How often/how many cases of treatment failure related to resistance have you seen?
7. All staff: Evaluate the effect of your workload on your ability to implement antibiotic stewardship activities.
8. Describe what (if any) antibiotic resistance has had on your practice.
9. Describe what (if any) antibiotic resistance has had on your community.
10. What do you think would be the most useful strategies to help decreases antibiotic use?

Tools and Technology

1. All clinicians: How do you determine a patient's antibiotic use status?

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a. What resources or tools do you use to decide which antibiotic is most appropriate for a patient?

2. Physicians and maybe pharmacists:
   a. How does the lab impact your antibiotic prescribing?
3. Lab staff: What changes could be made to your lab that would help you to more effectively support antibiotic prescribing/stewardship at your hospital?

Environment

What posters, signs, or other visual cues promoting good antibiotic prescribing are present in your hospital? Where are they located? Which ones do you notice most?

Final: Is there anything I haven't asked you about antibiotic stewardship that you think is important for me to know?

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Reporting checklist for qualitative study.

Based on the SRQR guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SRQR reporting guidelines, and cite them as:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. Acad Med. 2014;89(9):1245-1251.

		Reporting Item	Page Number
	#1	Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended	5
	#2	Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions	2
Problem formulation	#3	Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	3
Purpose or research question	#4	Purpose of the study and specific objectives or questions	2
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research) and guiding theory if appropriate; identifying the	5

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		research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	
Researcher characteristics and reflexivity	#6	Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability	n/a. The team did not feel any characteristics dramatically influenced our devising of the interview guide or the data collection.
Context	#7	Setting / site and salient contextual factors; rationale	4
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	5
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	6
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	5
Data collection	#11	Description of instruments (e.g. interview guides,	Appendix 1

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instruments and technologies		questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	
Units of study	#12	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	5
Data processing	#13	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	6
Data analysis	#14	Process by which inferences, themes, etc. were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	6
Techniques to enhance trustworthiness	#15	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	6
Syntheses and interpretation	#16	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	6
Links to empirical data	#17	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	18-22
Intergration with prior work, implications, transferability and contribution(s) to the field	#18	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	12
Limitations	#19	Trustworthiness and limitations of findings	12
Conflicts of interest	#20	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	1
Funding	#21	Sources of funding and other support; role of funders	1

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in data collection, interpretation and reporting

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Manuscripts

Evaluating Antibiotic Stewardship in a Tertiary Care Hospital in Kerala, India: A Qualitative Interview Study

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writing and editing the manuscript. AS helped with the grant and edited the manuscript. JK edited the manuscript.

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Abstract

Objectives: To determine what barriers and facilitators to antibiotic stewardship exist within a healthcare facility.

Setting: 1300 bed tertiary care private hospital located in the state of Kerala, India.

Participants: 31 semi-structured interviews and 4 focus groups with hospital staff ranging from physicians, nurses, pharmacists, and a clinical microbiologist.

Results: Key facilitators of antibiotic stewardship (AS) at the hospital included a dedicated committee overseeing appropriate inpatient antibiotic use, a prompt microbiology lab, a high level of AS understanding among staff, established guidelines for empiric prescribing, and an easily-accessible antibiogram. We identified the following barriers: limited access to clinical pharmacists, physician immunity to change regarding stewardship policies, infrequent antibiotic de-escalation, high physician workload, an incomplete electronic medical record (EMR), inadequate antibiotic stewardship program (ASP) physical visibility, and high antibiotic use in the community.

Conclusions: Opportunities for improvement at this institution include increasing accessibility to clinical pharmacists, implementing strategies to overcome physician immunity to change, and establishing a more accessible and complete EMR. Our findings are likely to be of use to institutions developing ASPs in lower resource settings.

Keywords: Antibiotic stewardship, antibiotic stewardship programs, antibiotic resistance, India, SEIPS

Strengths and limitations of this study

- Our study is the first of its kind to systematically examine the key barriers and facilitators of implementing an ASP in a low/middle-income country (LMIC).
- We interviewed a variety of healthcare workers: physicians, nurses, clinical pharmacists, and a microbiologist.
- This was a single center study. Thus, transferability of our findings to more resource-limited rural hospitals within India or to other LMIC may not be possible.
- We did not conduct direct observations of practice to correlate with self-reporting.

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Background

The United Nations declared antimicrobial resistance to be "the greatest and most urgent global risk" in 2016[1]. Antibiotic overuse and misuse drives antimicrobial resistance[2]. In India, rates of infections caused by antibiotic resistant bacteria are high and increasing[3-11]. Given that the main driver of antibiotic resistance is antibiotic use and misuse, antibiotic stewardship (AS) and antibiotic stewardship programs (ASP) have a critical role in promoting judicious antibiotic use[12].

In a recent review of AS studies spanning every continent, Davey et al. found ASPs were effective in decreasing treatment duration and increasing adherence to antibiotic use policy[13]. While the evidence for ASP effectiveness is growing, there is considerable variation among ASPs in size, activities, and scope. Newly published consensus of an ASP core elements checklist includes experts from twelve countries on six continents and should be considered by healthcare centers when considering their individual ASP, no matter their economic status[14]. This checklist includes some of the elements we identified as areas of strength in this institution: senior hospital management support, a formal ASP, and timely access to laboratory results. Still, we recognize low and middle income countries (LMIC) face

ASP implementation challenges including limited diagnostic lab capability, inadequate awareness, limited access to quality antibiotics, and high patient census[15]. To date, few studies have explored the challenges facilities in India face carrying out ASPs, such as less available manpower and money dedicated to maintaining a detailed electronic medical record (EMR) compared to higher income country counterparts[16-18]. EMR systems have been found to be one of the most effective ways of keeping records on patient care and allow for easier discussion and feedback on antibiotic choices[17]. We selected India because, as mentioned, antibiotic resistance rates are high and increasing, and our study facility had recently implemented an ASP to address this issue. Thus, we undertook a prospective qualitative study in Kerala, India to examine the barriers and facilitators to practicing AS in a LMIC healthcare setting and to identify opportunities to improve AS.

Methods

Location

In January 2018, we conducted a qualitative study to understand the barriers and facilitators to AS at a 1300 bed tertiary care private hospital located in the state of Kerala, India. This urban hospital, which includes 275 intensive care beds, provides free or subsidized advanced care for two-thirds of its patient population. AS activities began in 2015. The hospital's ASP, members of which include internists, surgeons, a microbiologist, critical care physicians, infection control nurses, and an administrator, began in 2016. The Chief Medical Officer, the head of both the institution as a whole and the ASP itself, initiated the antibiotic stewardship meetings, infectious disease rounds, chart review of patients. Committee members are a mix of junior, mid-level, and senior staff and serve for at least two years with the option to continue involvement afterward.

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Study population

Physicians, nurses, clinical pharmacists, and a microbiologist were identified by the on-site study team by emailing information to staff regarding the project and subsequently approached staff in-person to identify interested participants. We included senior faculty and healthcare professionals working on the critical care medicine and infectious disease teams for interview. Exclusion criteria included non-English speaking staff and staff who were subordinates to any member of the study team.

Data collection

We conducted 31 semi-structured interviews and 4 focus groups with hospital staff involved in AS. Interview guides were developed based on the Systems Engineering Initiative for Patient Safety (SEIPS) framework. This framework evaluates the interactions between the people, organization, tasks, tools/technology, and environment of a given work system, allowing for identification of key areas for improvement or intervention[19]. Interviews were conducted in private rooms at the hospital, and were audio recorded after obtaining verbal consent from the participant. No personal information was recorded, and each interview lasted between 10 and 30 minutes. The interview guides used have been included for reference (Appendix A).

Analysis

All interviews were transcribed and analyzed deductively using the SEIPS framework. One member from the study team manually coded the interview transcripts. Quotations from transcribed interviews were sorted into the SEIPS categories of person, organization, tasks, tools/technology, and physical environment. After all study team members agreed on the identified themes from the interviews, the most prominent barriers and facilitators to AS

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were identified in each category based on number of participant responses. We used the Standards for Reporting Qualitative Research (SRQR) guidelines[20].

Ethics approval

The Institutional Review Board at the University of Wisconsin-Madison granted this study exemption from full review. The Internal Ethics Committee at the participating hospital reviewed the study and granted approval (IRB# 2017-1268).

Patient and Public Involvement statement

The development of our study was informed by many patients' preference to get antibiotics right away, just in case these drugs help. This can influence how healthcare providers deal with prescribing. We did not involve patients with the design or conduct of the study. Results will be disseminated to the involved healthcare workers at staff meetings and electronic communications.

Results

In total, we interviewed 45 hospital faculty and staff. Participants included individual interviews with physicians (27), clinical pharmacists (3), and one microbiologist. We also conducted four focus groups consisting of ASP team members, pharmacists (two groups), and infection control nurses with two to five participants each.

Organization

The hospital's ASP is the key organizational component of promoting judicious antibiotic use and is in addition to the three clinical pharmacists and one infection control nurse the hospital uses as dedicated, full-time stewardship positions. The ASP team evaluates the list of inpatients receiving antibiotics to evaluate "The Five R's" of antibiotic prescribing: right drug, right dose, right frequency, right duration, and right indication. When

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the team identifies opportunities for antibiotic de-escalation or reduced duration, a clinical pharmacist member contacts the prescribing physician to issue treatment recommendations, and the prescribing physician decides whether to modify treatment. Typically the hospital sees 30 "higher antibiotic" prescriptions a day; these are the cases the ASP reviews. Usually the committee has suggestions for five or six cases, most often communicating these with staff via email for recording/tracking purposes. In-person communication during rounds, telephone calls, and text messages to the microbiologists in the lab are also utilized as they are more effective methods of quick communication.

According to about half of respondents, hospital administrative leadership champions the ASP by being involved in the meetings, handling difficult conversations with physicians, and instilling confidence in all staff that the ASP is working with them to improve patient care. Staff in turn view their institution's ASP as a key facilitator of AS at the hospital (Table 1, quotes 1-3). In addition to the ASP itself, 17 interviewees regarded the microbiology lab as a key facilitator of AS. Staff praised the 24-hour lab's promptness and the rapidity with which lab staff uploaded results into the EMR. In addition, many physicians relied on the microbiologist's expertise for help identifying microorganisms in complicated infections (Table 1, quotes 4 and 5). As one physician said, "If we are thinking about a gram positive illness and we get a culture that's gram negative, which is grown very quickly, we totally change our report."

Despite having an effective stewardship program and lab, 16 interviewees identified limited clinical pharmacist availability as a barrier to AS. In India, clinical pharmacists must complete a six year Doctorate program from an accredited university to receive licensure, and many physicians recognized clinical pharmacists' knowledge as a critical component of

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patient care. However, several departments had one clinical pharmacist and many had none at all. Staff worried this lack of pharmacist access may cause clinicians to miss drug interactions or prescribe antibiotics at incorrect dosages (Table 1, quotes 6-8).

Person

During our interviews, staff identified AS activities, such as using the correct antibiotic at the correct dose, as a key component of reducing antibiotic resistance. In addition, staff mentioned they often heard about AS at work. This high level of awareness among staff facilitates AS practices (Table 1, quotes 9-11).

While most interviewed staff demonstrated AS policy understanding, they revealed many physicians resisted accepting suggestions from the ASP. Moreover, several physicians and pharmacists worried other physicians did not acknowledge pharmacists' contributions to patient care. According to nine interviewees, this immunity to change may impede AS practices and contribute to antibiotic resistance through incorrect antibiotic dosing and duration (Table 1, quotes 12 and 13). One clinician described this phenomena for us by saying, "I think clinicians are empowered to think that they know best. They need to recognize the roles of the microbiologists and the pharmacists and should not feel low that they have asked for help." A nurse we spoke to distilled the issue; "Challenges come from navigating human behavior." Staff immunity to change may present challenges for other LMIC as well; strategies which have been helping this particular facility are publishing easily accessible guidelines and committing to persistent interaction between staff and the ASP. In this way, AS is a priority which is tended to and fostered as an institution-wide value.

Tasks

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Staff in 12 interviews felt that clinicians follow established guidelines when prescribing antibiotics when the cause of illness is not yet known. Following a clinical evaluation, the physician orders a culture and initiates a broad-spectrum antibiotic. Physicians then use this culture result to modify the original antibiotic used. This process, often called de-escalation, involves selecting an antibiotic which has a more specific spectrum or stopping antibiotic treatment if the cultures do not identify a bacterial infection (Table 1, quote 14).

As a tertiary care facility, this hospital frequently treats high-risk patients who have acquired resistant infections in the community or at other hospitals. Therefore, physicians at our study institution often feel compelled to empirically prescribe broad-spectrum antibiotics while awaiting culture results. However, physicians often forget or refuse to de-escalate antibiotic use due to workload or fear of losing the patient. In our study, physicians and pharmacists in eight interviews worried this lack of de-escalation may increase the risk of antibiotic resistant infections (Table 1, quote 15) and cited de-escalation as the most important issue regarding antibiotic prescribing. Similarly, nine interviewed staff members feared their high workloads may negatively impact their ability to always judiciously prescribe antibiotics. Physicians noted they are often unable to spend sufficient time evaluating a patient and this, along with uncertainty over what exact drugs the patient has already taken pre-admission, leads to antibiotic over-prescription (Table 1, quotes 16 and 17). This happens because if a patient has already taken a certain class of antibiotic and they haven't worked, prescribing more is not going to help.

Tools/Technology

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The hospital microbiologist and clinical pharmacists update the hospital antibiogram annually. The antibiogram, which gives the percent of pathogens susceptible to various antimicrobial agents, is accessible on the hospital intranet and divided into Gram positive, Gram negative, and yeast. In 17 interviews, staff members identified this user-friendly tool as a key facilitator in selecting antibiotics based on hospital resistance patterns, a critical component of AS (Table 1, quote 18).

In addition to the antibiogram, this hospital also utilizes an EMR, which to save money is built and maintained by the hospital's Information Technology department. The EMR is used to store information on inpatients, a useful addition for identifying immediate drug interactions and thereby reducing harm. However, the EMR does not contain a patient's full scope of antibiotic use, including antibiotic history, duration, and dose. This incompleteness often forces physicians and pharmacists to refer to a patient's paper health record, which one pharmacist described as a "tedious" process (Table 1, quote 19). Moreover, physician workflow does not include entering antibiotic data into the EMR. Due to high work volume, physicians depend on the ward secretary, nursing assistants, or research assistants to update the EMR. As one physician explained, "I see 80 patients a day. So it's not possible for me to spend so much time logging in, recording all this. I don't think it's possible unless I had someone sitting next to me doing just that." (Table 1, quote 20). A dozen interviewed staff members identified this inability to quickly access the full scope of a patient's antibiotic history as a barrier to judiciously prescribing antibiotics.

Environment

Despite having a highly engaged AS team, staff mentioned the hospital did not have signs or posters to increase stewardship awareness, which several staff identified as a

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potentially useful addition. A few interviewees thought AS policies were sometimes printed and posted but did not "stand out." These printed antibiotic prescribing protocols were not visible to all staff, and 23 interviewed staff members mentioned this limited visibility may inhibit widespread AS awareness. (Table 1, quotes 21 and 22)

In addition, staff identified high local antibiotic use as a barrier to stewardship. As patients can purchase antibiotics over the counter or have been recently hospitalized at another facility, many patients enter the hospital already using antibiotics. These high use rates often lead to antibiotic resistant infections in the community, forcing physicians to prescribe broad-spectrum antibiotics. Furthermore, several staff feared the impact of high antibiotic use in animal husbandry and fisheries on spreading resistance. Seven staff members wished for enhanced antibiotic prescribing regulations and more AS awareness in greater India (Table 1, quote 23).

Discussion

Our study is the first of its kind in the English language to systematically examine key barriers and facilitators of implementing ASP in a LMIC tertiary hospital. Using the SEIPS model, we examined the implementation of an ASP at a large tertiary care hospital in order to identify opportunities to improve this program.

We found that limited access to clinical pharmacists, physician immunity to change resulting in infrequent antibiotic de-escalation, high physician workload, an inadequate EMR, inadequate physical visibility of stewardship activities, and high antibiotic use in the community were major barriers to effective ASP implementation. The presence of a prompt microbiology laboratory, high level of understanding of AS among staff, easily accessible antibiogram, and established guidelines for empiric prescribing were identified as important

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facilitators of an effective ASP in this hospital. As Ravi et al. (2017) discovered, we found committed leadership from the administrator was a major factor as well[17]. This could be a main driver of why AS understanding and opinions about the facility's AS efforts were fairly unified among interviewees regardless of if they were involved in the ASP team or not.

Our study found limited access to pharmacists was a barrier for an effective ASP. Multidisciplinary rounds with guideline-based antibiotic recommendations for specific infections have been found to decrease use and duration of both broad spectrum and high-end, reserve antibiotics[21]. Clinical pharmacists can provide real-time decision support which could significantly improve rates of antibiotic tailoring to culture data[22]. Empowering clinical pharmacists to identify highly misused antibiotics, design guideline-based de-escalation protocols, and participate in multidisciplinary rounds may improve the quality of ASP.

Physician resistance to changes in antibiotic use practices was identified as a barrier to an effective ASP. Factors which influence physician antibiotic prescribing habits include anxiety about missing an infection and the antibiotic prescribing behavior of peers[23]. This is an important active area of research; interventions such as encouraging reflection on practice, the use of audit and feedback, small-group learning with discussions and engagement by senior clinicians, and deploying multidisciplinary teams including clinical pharmacists have been shown to improve prescriber behavior[24,25]. In LMIC settings, we recommend leadership should actively promote ASP activities and their value. Feedback on antibiotic usage and patterns should be disseminated to improve adherence to local or national guidelines at this facility.

We found that the usability and accessibility of the EMR were another barrier to an effective ASP. Adoption of an EMR can improve ASP by providing a centralized location for

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microbiology results and other relevant clinical data[26]. However, the expense of acquiring and optimizing an EMR system to harness its full potential makes this intervention difficult to implement, particularly in LMIC settings[27].

Our study identified high and indiscriminate community-based antibiotic use as one reason why AS is such a challenge at our study site. Variably-enforced regulations on antibiotic dispensing and the availability of antibiotics without a prescription is a widespread problem in many countries, including India[28]. The broad and unregulated use of antibiotics in animal feed and fisheries compounds this barrier[29]. ASP in healthcare settings can be complemented by AS in the community for all uses of antibiotics, with an inclusive "One Health" approach to addressing resistance[30]. While not mentioned by any staff, extensive pollution from pharmaceutical production has also been noted as a driver of resistant bacteria, and this too should be addressed in a One Health approach[31]. The state which our study institution exists, Kerala, is currently the only state in India to have an antibiotic policy. Efforts for federal antibiotic use regulations have some support, but nothing has yet come to fruition.

Our study has limitations. First, this was a single center study. Thus, transferability of our findings to more resource-limited rural hospitals within India or to other LMIC may not be possible. Second, we did not conduct direct observations of practice to correlate with self-reporting. Future studies may identify additional barriers and facilitators by implementing direct observation approaches to collect data on stewardship practices. We also asked staff members if they would like to be interviewed, thus introducing the possibility only those who were really invested in AS would agree.

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Conclusion

The use of the SEIPS model to analyze an ASP in an LMIC identified barriers and facilitators within the healthcare work system. Opportunities for improvement at this institution include increasing accessibility to clinical pharmacists, implementing strategies to overcome physician immunity to change, and establishing a more accessible and complete EMR. Interventions which account for and address barriers and strengthen facilitators should be tested in future studies for their effect on antimicrobial usage and resistance.

Author Statement

KB created the interview guides, conducted in-person interviews, and wrote, edited, and prepared the manuscript. CS created the interview guides, conducted in-person interviews, and wrote/edited the manuscript. JK edited the manuscript. LK conducted on-site data collection and wrote/edited the manuscript. MVJ assisted with on-site data collection and edited the manuscript. SS devised the project and edited the manuscript. NS obtained funding, devised the project, and edited the manuscript. AS assisted with the grant and edited the manuscript. DS assisted with the grant and wrote/edited the manuscript.

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Table 1. Themes identified from SEIPS components with corresponding representative quotations

Theme	Representative Quote
Organization	
Antimicrobial Stewardship Program	1. "We audit to make sure the right indication is happening. We check to see the dosage is correct and monitor what's happening here to track our prescriptions." (pharmacist)
	2. "Every year we do something with the antibiotic prescription program. Along with infection control. Usually a three-day program for doctors and one day is dedicated to antibiotic stewardship. Speakers from all over the country [come] and we take about 30-35 doctors a year and try to teach them about antibiotic stewardship." (infection control nurse)
	3. “The medical superintendent is a part of our team. I don’t think you can get much higher up than that. The management is very supportive.” (pharmacist)
Microbiology laboratory	4. "Our microbiology lab is one of the best in the country. They are very reliable and help us immensely." (physician)

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	5. “Whenever the lab grows something in the culture, could be six hours, ten hours, we are called and told. So that does impact our management. If we are thinking about a gram positive illness and we get a culture that’s gram negative, which is grown very quickly, we totally change our report. We are informed pretty quickly.” (physician)
Clinical pharmacist availability	6. “[Pharmacists are] not routinely in the ICU. I wish more pharmacists would tell physicians their doses or their drug interactions are wrong, but I don’t see them in the cardiac or pediatric ICU.” (physician)
	7. “We have one pharmacist in our ICU, she visits. The problem with her is she’s overworked. She’s alone. She comes on the rounds only sometimes and comes around and checks the antibiotics dosing is correct. But duration and all others are decided by physicians. If there were more of them it would be much better.” (physician)
	8. “If a clinician is working alone, we may not have much concern about things that pharmacists are more aware of, like drug interactions. Routine medications may have interactions also, so pharmacists’ help is needed. That type of information is more with the pharmacists, not the clinicians. They are not always available.” (physician)
Person	
Antibiotic stewardship knowledge	9. “Antibiotic stewardship is a standardized practice with the right treatment at the right time.” (physician)

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	10. “To me antibiotic stewardship is to start judicious antibiotics…I won’t say to start low antibiotics, I say to start optimum antibiotics.” (physician)
	11. “Most of us here are aware of these ideas. For us, it’s about everything that has to do with a prescription. The ultimate aim is judicious use of antibiotics. We need to use the right antibiotics, the right dose.” (physician)
Physician resistance to antibiotic stewardship policies	12. “I think clinicians are empowered to think that they know best. They need to recognize the roles of the microbiologists and the pharmacists and should not feel low that they have asked for help.” (physician)
	13. “Challenges come from navigating human behavior. Sometimes you’ll recommend things but people just won’t listen to you.” (infection control nurse)
Tasks	
Antibiotic prescribing	14. “We have a high patient load and socioeconomic status is a big deal. Poverty and malnourished children are a reality. We can’t wait for cultures. We have protocols to start them on antibiotics according to which ones have been most successful here.” (physician)
	15. “I think it’s a problem all over India, because the first antibiotics they prescribe is the carbapenems. And once they prescribe it is never de-escalated or rarely de-escalated. Basically they go, ‘let’s continue. What the culture says? I don’t want to do that. Let’s just continue because he’s improving.’ So it’s a major, major, major problem.” (physician)

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Workload	16. "Sometimes we are busy and we forget pre admission drugs which are missed because we are more worried about the current problems, and there are so many the patient is already on, that we need to continue." (physician)
	17. "Our work here does affect how long you can spend on individual cases." (infection control nurse)
Tools and Technology	
Antibiogram	18. "It is an annual antibiogram. We divide it into gram positive, gram negative, and yeast. We also have a blood gram positive from blood isolates, negative, and yeast. They are separate. We follow international guidelines so for any isolate that is more than 30, we take them and follow the rules. Every year it is updated. This year they are trying to involve more pharmacists" (infection control nurse)
Electronic medical record	19. "If I look today at the record, I can only see what they took today. The current medications only. Not what they got yesterday. I can't trace the meropenem. To see all the drugs we have to go to the paper medical record room. It's a very tedious process. We don't know the dose or duration or all the drugs…if the patient returns in a few weeks, we don't know what they were taking and what will be effective." (pharmacist)
	20. "I see 80 patients a day. So it's not possible for me to spend so much time logging in, recording all this. I don't think it's possible unless I had someone sitting next to me doing just that." (physician)

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Environment	
Posters or signs promoting antibiotic stewardship awareness	21. "It's only in protocols, which we do print out only for doctors. Nurses don't see that." (physician)
	22. "We have some print-outs on our notice board about colistin and other higher-end antibiotics…but we don't have posters. As for the printouts, they aren't that catchy." (physician)
High levels of community antibiotic use	23. "Outside the hospital this is a rampant problem in India. There is much abuse and misuse of antibiotics. Anyone can just go to a roadside pharmacy and describe their symptoms and get antibiotics over the counter just like that. They just go to the guy sitting there and get whatever. I think we should make it much harder to get antibiotics." (physician)

Frequently used abbreviations:

LMIC: low and middle income countries

ASP: antibiotic stewardship program

AS: antibiotic stewardship

SEIPS: Systems Engineering Initiative for Patient Safety

EMR: electronic medical record

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Appendix A: Antibiotic Stewardship Interview Questions

Interviewer: Antibiotic stewardship refers to the judicious use of antibiotics, and is a critical component of reducing antibiotic resistance. Components of antibiotic stewardship involve drug expertise, evaluating ongoing antibiotic treatment, monitoring prescribing practices, and reporting information on antibiotic use and resistance.

Your responses will be recorded with a voice recorder and transcribed, but the responses will be de-identified in any data set and your identity will be kept confidential.

Person

1. How do you define antibiotic stewardship?
2. What do you think of antibiotic stewardship as an infectious disease prevention strategy?
3. Describe your level of interaction working with infectious disease specialists at your hospital.
4. Physician/Nurse
    a. Describe your work with pharmacists in your hospital.
        i. If poor availability/they don't work with pharmacists: What factors limit their availability to you?
        ii. How do you work with pharmacists on specific patients?
        iii. In an ideal situation, what would be different about how you work with the pharmacists?
    b. Tell me about your workload.
        i. How does your workload impact your ability to complete your job responsibilities?
5. All clinicians: Describe employee turnover on your ward

Organization

1. Describe your experience regarding antimicrobial stewardship education in your facility.
    a. What is your view of these trainings (how likely are you to attend? Do you apply the information to your practice? Who attends?)?
2. What do you hear about antimicrobial stewardship at work?
3. Describe a time a new policy was implemented on your ward/in your lab.
    a. What challenges were encountered? What went well? How did this compare to other times when new policies were implemented?
    b. How were staff involved in the development of the new policy? How are they typically involved in policy development
4. Tell me about your interactions with people involved in the antibiotic stewardship program.
    a. What types of things do you collaborate on/communicate about?
    b. How could your interactions be improved?
5. What is your sense of how hospital leaders/management are involved in antibiotic stewardship efforts in your ward/lab?

6. All clinicians: How could antibiotic prescribing be improved in your facility? Tell me about empiric prescribing at your hospital. What factors should be considered when prescribing an antibiotic if the cause of illness is not yet known?

Tasks

1. Lab Staff
    a. Describe how you create an antibiogram.
        i. How does creating an antibiogram fit in with your other job responsibilities?
        ii. How often do you update the antibiogram?
        iii. What is the scope of the antibiogram?
2. Nurses
    a. What antibiotic stewardship practices are you responsible for on your ward?
    b. How often do you review medications? Describe your review process.
    c. What do you do when antibiotic usage seems questionable? Do you or your team decide together?
    d. Are routine audits of antibiotic use conducted on your ward?
3. Pharmacists
    a. What is your process when an antibiotic is ordered?
        i. What are your selection review practices? Describe your collaboration with physicians.
        ii. Describe your antibiogram use, including successes and challenges. How frequently is it updated?
4. Physicians
    a. Describe your antibiotic selection process, including any guidelines you may use in making your decision.
        i. Describe your antibiogram use, including successes and challenges. How frequently is it updated?
        ii. How often are those guidelines adhered to in your workplace? If infrequently, what are the barriers to adherence?
    b. Describe your review of antibiotic selection, including after the drug has been prescribed and after you have obtained culture results.
5. All clinicians: Where do you store information on antibiotic use (dosage, duration, indication)?
6. All clinicians: How often/how many cases of treatment failure related to resistance have you seen?
7. All staff: Evaluate the effect of your workload on your ability to implement antibiotic stewardship activities.
8. Describe what (if any) antibiotic resistance has had on your practice.
9. Describe what (if any) antibiotic resistance has had on your community.
10. What do you think would be the most useful strategies to help decreases antibiotic use?

Tools and Technology

1. All clinicians: How do you determine a patient's antibiotic use status?

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a. What resources or tools do you use to decide which antibiotic is most appropriate for a patient?

2. Physicians and maybe pharmacists:
   a. How does the lab impact your antibiotic prescribing?
3. Lab staff: What changes could be made to your lab that would help you to more effectively support antibiotic prescribing/stewardship at your hospital?

Environment

What posters, signs, or other visual cues promoting good antibiotic prescribing are present in your hospital? Where are they located? Which ones do you notice most?

Final: Is there anything I haven't asked you about antibiotic stewardship that you think is important for me to know?

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Reporting checklist for qualitative study.

Based on the SRQR guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SRQR reporting guidelines, and cite them as:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. Acad Med. 2014;89(9):1245-1251.

		Reporting Item	Page Number
	#1	Concise description of the nature and topic of the study identifying the study as qualitative or indicating the approach (e.g. ethnography, grounded theory) or data collection methods (e.g. interview, focus group) is recommended	5
	#2	Summary of the key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results and conclusions	2
Problem formulation	#3	Description and signifcance of the problem / phenomenon studied: review of relevant theory and empirical work; problem statement	3
Purpose or research question	#4	Purpose of the study and specific objectives or questions	2
Qualitative approach and research paradigm	#5	Qualitative approach (e.g. ethnography, grounded theory, case study, phenomenolgy, narrative research) and guiding theory if appropriate; identifying the	5

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		research paradigm (e.g. postpositivist, constructivist / interpretivist) is also recommended; rationale. The rationale should briefly discuss the justification for choosing that theory, approach, method or technique rather than other options available; the assumptions and limitations implicit in those choices and how those choices influence study conclusions and transferability. As appropriate the rationale for several items might be discussed together.	
Researcher characteristics and reflexivity	#6	Researchers' characteristics that may influence the research, including personal attributes, qualifications / experience, relationship with participants, assumptions and / or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results and / or transferability	n/a. The team did not feel any characteristics dramatically influenced our devising of the interview guide or the data collection.
Context	#7	Setting / site and salient contextual factors; rationale	4
Sampling strategy	#8	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g. sampling saturation); rationale	5
Ethical issues pertaining to human subjects	#9	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	6
Data collection methods	#10	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources / methods, and modification of procedures in response to evolving study findings; rationale	5
Data collection	#11	Description of instruments (e.g. interview guides,	Appendix 1

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instruments and technologies		questionnaires) and devices (e.g. audio recorders) used for data collection; if / how the instruments(s) changed over the course of the study	
Units of study	#12	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	5
Data processing	#13	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymisation / deidentification of excerpts	6
Data analysis	#14	Process by which inferences, themes, etc. were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale	6
Techniques to enhance trustworthiness	#15	Techniques to enhance trustworthiness and credibility of data analysis (e.g. member checking, audit trail, triangulation); rationale	6
Syntheses and interpretation	#16	Main findings (e.g. interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	6
Links to empirical data	#17	Evidence (e.g. quotes, field notes, text excerpts, photographs) to substantiate analytic findings	18-22
Intergration with prior work, implications, transferability and contribution(s) to the field	#18	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application / generalizability; identification of unique contributions(s) to scholarship in a discipline or field	12
Limitations	#19	Trustworthiness and limitations of findings	12
Conflicts of interest	#20	Potential sources of influence of perceived influence on study conduct and conclusions; how these were managed	1
Funding	#21	Sources of funding and other support; role of funders	1

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