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Antibiotic use, environment and antibiotic resistance: A qualitative study among human and veterinary health care professionals in Orissa, India.

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Abstract

Objective: To explore views of medical doctors, veterinarians and drug sellers on use of antibiotics on humans and nonhumans and on factors that influences the development of resistance to antibacterial agents. Further, to look at the bi-directional relationship between antibiotic use and environment.
Methods: The study was a qualitative explorative interview study, analysed using conventional content analysis. It was conducted in Orissa, India. Data were collected by face to face semi structured interview. The interviews were tape recorded and transcribed into Oriya, then translated in to English. Each paragraph or sentence was coded. Similar codes were clustered together and collapsed into sub categories and categories. The main themes were allowed to emerge, based on the relationship between categories.
Findings: The main finding of the study was mishandling and abuse of antibiotics in patients as well as at professional level due to weak implementation of legislation, which appears to be the major cause of antibacterial agent resistance. Incomplete course or dose due to poverty in rural area and self medication in urban area are more common. The study also showed that climatic factors, pollution and population density are the major ecological factors which influence antibiotic prescriptions. Another major finding of this study was that, due to improper disposal system of pharmaceuticals; antibiotics are contaminating air, water and terrains which can cause major risk to aquatic and grazing animals.
Conclusion: This study emphasises the need for comprehensive actions including information, training, legislation and education at all levels of drug delivery system to rationalize antibiotic use by improving prescribing pattern and creating awareness among consumers. Proper disposal of pharmaceutical wastes is required to prevent the contamination of environment from pharmaceutical pollutants. Further study is essential concerning environmental impact of antibiotics.

Key words: Antibiotic use; antibiotic resistance; environment; qualitative; conventional; content analysis; veterinarians; medical doctors; drug sellers; Orissa; India.

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Introduction

Background of the Study

Mortality as a result of infectious diseases represents one-fifth of global deaths [1]. The success of antibiotics against diseases caused by microbes is great achievements in modern medicine. Over the years, antibiotics have saved the lives and eased the suffering of millions of people. Currently, pathogenic bacteria are becoming resistant to antibiotics at an alarming rate. It is frequently recognized that the widespread misuse of antibiotics in human health, veterinary, aquaculture, agriculture and household products, represent an important reason for the increase in antibiotic resistance [2,3,4,5]. Due to enormous growth of global trade and travel, both infectious diseases and resistant microorganisms spread between continents [2]. Antibiotic resistance has been called one of the World's most burning public health problem affecting both current and future generations.

Antibiotic resistance is the ability of bacteria to resists the effect of an antibiotic. As per the previous literature review study *Salmonella enterica* resistant to ampicilin, choramphenicol and cotrimaxazole*; Vibrio cholerae* strains resistant to cotrimoxazole and tetracycline; *Campylobacter* species resistant to fluoroquinolone; and *Streptococcus pneumonia* resistant to penicillin, chloramphenicol, tetracycline and erythromycin; *Mycobacterium tuberculosis* resistant to multi-drug therapy are reported [6].Above study indicates that antibacterial resistance is the pressing public health problem.

The nonhuman use of antibiotics include; veterinary, agriculture, aquaculture and as growth promoters in pig and poultry production. As per the World Health Organization (WHO) report, various antibiotics are licensed and used in fish and shrimp production; and half of the total amount of antibiotics produced globally is put for nonhuman use [5]. All antibiotics used in veterinary medicine are the same or closely related to antibacterial used in human medicine and that's why they induce cross-resistance [7]. The widespread misuse of antibiotics in nonhumans are creating serious problem in human health care system. Due to this reason WHO strongly recommends that antibiotics used for treating infections in humans should not be used as growth promoters in animals. Sweden banned the use of all animal growth promoters in 1986. In the year 1997 European Union encouraged, banning of all antimicrobial animal growth promoters which are used in human medicine [5].

Environmental factors have significant impact on antibiotic use. Both abiotic and biotic factors affect the human health. Due to climate change, pollution and high population density the micro-organisms are rapidly spreading in the surroundings and are impacting human health, hence antibiotic prescriptions. The literature review showed that there is not any scientific study on influence of ecological factors on antibiotic prescriptions.

Around the world, thousands of tons of pharmaceuticals are used annually but little is known about the ultimate fate and potential effect of several drugs after their intended use. Recently few studies have demonstrated that many pharmaceuticals are incompletely eliminated at sewage treatment plants and some antibiotics are found in municipal waste water, surface water and agriculture waste [8,9,10,11,12]. The literature review showed that there is no published qualitative

study on environmental impact of antibiotics. A major concern so far has been that antibiotics found in aquatic environment may cause increased resistance among natural bacterial populations. Antibiotics remain biologically active even at low levels, so their impact and environmental interaction can be much subtler and complex than many contaminants. Therefore, antibiotics and its ingredients in the aquatic environment are warning signals for current and future public health as well as ecological problems. Qualitative study is necessary to explore the community response and consciousness regarding environmental issue of antibiotics.

Due to resistance, scientists are trying to create new antibiotics to replace old ones. In recent years, the pharmaceutical industry has produced few new drugs. On average, research and development of a single new antimicrobial takes 10-20 years and costs US $ 500 million dollars to bring into the market [13]. The rise of antibiotic resistant bacteria is a major public health crisis as infections from resistant bacteria are becoming increasingly difficult and expensive to treat. When bacteria become resistant to first line antibiotics, treatment has to be switched to second or third line drugs, which are generally expensive [2]. Many of second and third line therapies for drug resistant infections are unaffordable due to their high price. Over the last decade, almost, every type of bacteria has become resistant and less responsive to antibiotic treatment when it is really needed. That's why more research and law for prudent use of antibiotic is essential.

Antibiotic resistance is a global problem. In Asia resistance problem is prominent [6] and in India the consequences of antibacterial resistance will be severe. There is rapidly growing pharmaceutical industry [14] and also high use of antibiotics in India. The economic capability to use second or third line antibiotics in cases where bacteria have developed resistance to first line treatment is lacking for ordinary people. Lack of surveillance and consequent late detection of resistant strains can further aggravate the situation. As per my knowledge, there is a lacuna of information regarding health care professionals' perception on antibiotic resistance and environmental impact of antibiotic use in Orissa, India. Due to this reasons we took a qualitative study to explore the views of human and veterinary health prescribers along with dispensers on antibiotic resistance; and to develop intervention for policymakers.

A qualitative research is the collection, analysis and interpretation of comprehensive narrative data in order to gain insights into a particular phenomenon of interest. Qualitative variable is not quantifiable. It depends upon attributes. It is useful for describing and answering questions about participants and contexts. It explains how economic, political, social and cultural factors influence health and society, i.e. environmental and organizational factors. While qualitative approaches assess in discovery of categories and define interpretation of different objects, quantitative approaches help to count and analyse them statistically [15]. Qualitative content analysis is used to organize the results according to emerging themes. It is a research method for the subjective interpretation of the content of the text data through the systematic classification process of coding and identifying themes or patterns.

Literature Review

Infectious diseases have the potential, like no other group of diseases, to spread rapidly over large distance in a short time. Due to overuse and misuse of drugs, bacterial resistance to antibiotics is accelerating at a disturbing rate around the world. According to WHO report most of the rising

antimicrobial resistance problem in human medicine is due to the overuse and misuse of antimicrobials by doctors, other health personnel and patients. Education on antimicrobial resistance and prudent antimicrobial use is lacking amongst dispensers and prescribers of antimicrobials [5]. Previous study in India declares, rising antibiotic resistance problems, largely due to wide spread and irrational use of antimicrobial agents in hospitals and the community in developing countries. Antibiotic resistance increases not only the healthcare costs, but also the severity and death rates from certain infections, that could have been avoided with prudent antibiotic use [16]. The spread of penicillin-resistant *pneumococci* and multi drug resistance tuberculosis is due to airborne transmission. Large numbers of commercial preparations, unethical drug promotions by pharmaceutical houses and irrational prescribing habits of clinicians are the important reasons for irrational prescription of drugs in clinical practice [17].

As per the previous study, self-medications with antimicrobials are another major factor contributing to resistance [2]. Self-medication percentage is high in urban areas in comparison with rural area [18]. Similar study in Europe elucidates that there are significant differences in levels of public attitudes, beliefs and knowledge concerning antibiotic use, self medication and antibiotic resistance. Awareness about antibiotic resistance was the lowest in countries with higher prevalence of resistance [19]. Patients who self-medicated were more likely to use an inadequate drug or dose [20]. A qualitative study on self-medication in Latine America points out, that patients believes that visit to physician for a diagnosis and prescription were unnecessary when the patient was familiar with the symptoms and it had previously responded to antibiotic treatment [21]. In Trinidad and Tobago, inappropriate use of antimicrobials resulted from self-medication, over the counter availability at the community pharmacy, prescribing on demands, and lack of regulatory control [22].

Antibiotic resistance is a major public health problem in Europe and worldwide. Its spread is partially due to inappropriate antibiotic consumption at the human and animal level and this can be controlled through better use of these antibiotics and their harmonised surveillance [23]. In developing countries complex socioeconomic and behavioral factors are associated with antibiotic resistance. There is a misuse of antibiotics by health professionals, unskilled practitioners, and laypersons; poor drug quality; unhygienic conditions accounting for spread of resistant bacteria; and inadequate surveillance [24]. Explanations of distinction between virus and bacterium often led to perceived confusion [25]. In both France and Britain about 90% of the patients receive antibiotics for tonsillopharyngitis [26]. Similar study on South India showed that purulent discharge, fever and patient satisfaction were the strong influences to prescribe an antibiotic; and belief of prescribing a broad spectrum antibiotic [27]. According to WHO, in many countries, including several developed countries, antimicrobials are available over-the-counter and may be purchased without prescription [5]. Similar study in Kerala, India, explains 20% of the antibiotics are purchased without doctor prescription, out of one thousand people four are engaged in unsupervised self-medication using antibiotics. The most commonly used groups of drugs are tetracycline, ampicillin, coxacillin and amoxicillin; cephalexins and ciprofloxacin taken in acute respiratory illness [28]. Previous study in Latin America enlighten there is lack of physician training on consumer's education on antibiotic use and abuse and its consequences [29]. Public knowledge regarding antibiotics is typically poor [30]. Similar study from nine African countries suggest that, since most people purchase their drugs from unqualified drug sellers, educating these drug sellers would probably be even more beneficial for public health in many low-income

countries [31]. A cross sectional study in Zimbabwe shows that, there is a low sale of antibiotics without prescription which is in sharp contrast to other studies from low income countries [32]. Non-prescribed use of antibiotics is very low in Sweden compared with other European countries [33].

The nonhuman use of antibiotics includes therapeutic, prophylactic and growth promotion use in food producing animals, agriculture, horticulture, aquaculture and industrial use. A recent review in Europe has revealed that an average amount of 100milligrams of antimicrobials are used in animals for production of one kilogram of meat for human consumption [5]. Generally the antibiotics used in veterinary medicine are fluroquinolone, penicillin, tetracycline, chlorotetracycline [7,34,35], cephalosporin [7,36,37], procaine penicillin dihydrostreptomycin, trimethoprim sulphonamides [38] and virginiomycin [34]. A pervious study in the United States showed that, a significant source of antimicrobial resistant food borne infections in humans is due to acquisition of resistant bacteria originating from animals [39].

There is a potential environmental impact of antibiotics. Antibiotics are entering in large quantities into the environment. According one study, the primary pathway of antibiotics into the environment is the use and disposal of out-of-date or unwanted medicines whose ecotoxicologic consequences with their presence are less clear [40]. As per a study in Patancheru, which is a major production site of the generic drugs for the world market near Hyderabad in India, high levels of several broad spectrum antibiotics specifically ciprofloxacin are present in aquatic environment [10]. A degree of multiple antibiotic resistances was observed in seven different *Vibro* species in the coastal water of Bay of Bengal at Orissa coast [41]. Antibiotics have been detected in surface water in many countries such as Canada, Germany, United States and other European countries [42]. A study in Australia mentions presence of three antibiotics i.e. ciprofloxacin, norfloxacin and cephalexin both in sewage effluent and environmental waters downstream from a sewage discharge. [11]. As per an earlier study in Germany in surface water, out of fourteen pharmaceuticals, 30% are antibiotics [12] and the sewage water also contains antibiotics and its degraded compounds [43]. In Spain, *Enterobacteriaceae* and *Aeromonas* spp. fresh water bacteria are resistant to nalidixic acid, quinolones and tetracycline [44].

Purpose of the Study

To explore views of medical doctors, veterinarians and drug sellers on use of antibiotics in humans and nonhumans and on factors that influence development of resistance to antibacterial agents. Further, to look at the bi-directional relationship between antibiotic use and environment.

Methods

Study design

The study was a qualitative explorative interview study, analysed using conventional content analysis. Conventional content analysis is generally used to describe a phenomenon. Content analysis is used to provide knowledge and understanding of phenomenon under study [47].

Study area

The study was conducted in Orissa, India (Figure 1). Orissa is located on the east cost of India. It has a population of 32 million, which is about four percent of the population of India. About 87% of the population lives in villages, out of which 25% are tribal. It extends over an area of 155,707 square kilometers accounting for 4.9 percents of the total area of India [50].

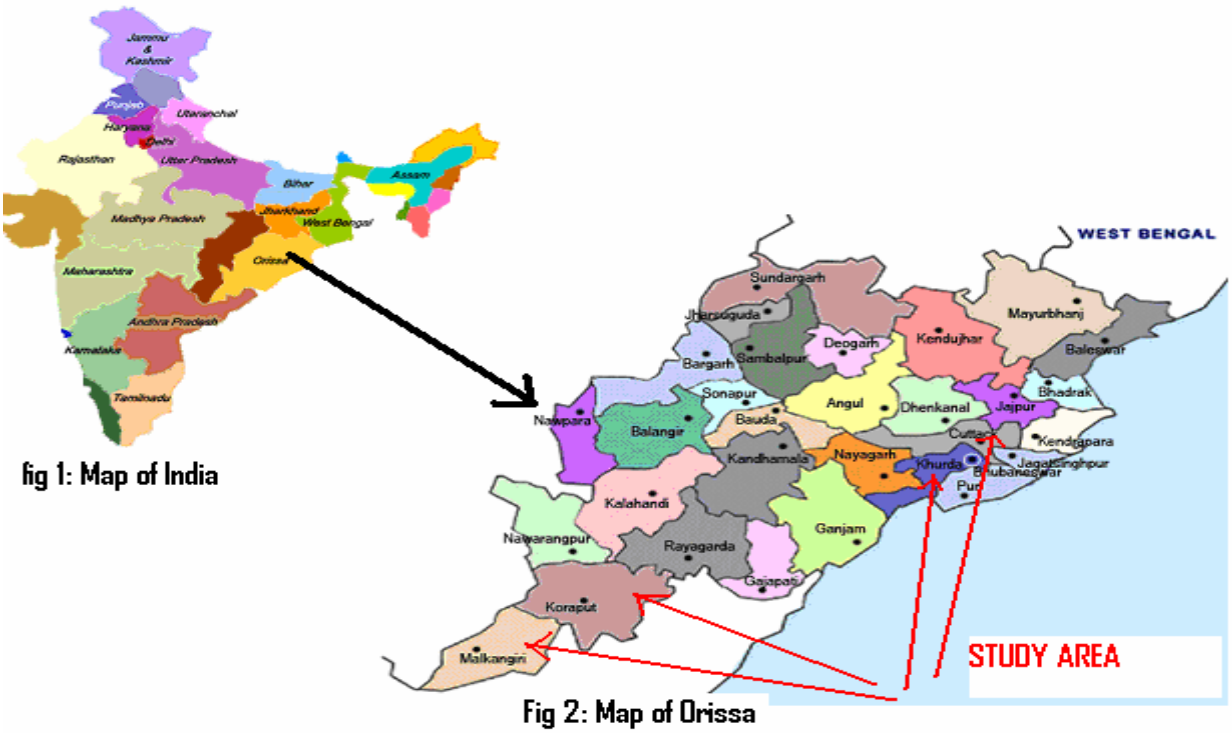

Fig 3: Study area in Orissa, India.

Out of the 30 districts of Orissa, four districts were selected for the study (Figure 2) with the intention of bringing in variety in sampling, based on the economy of the people and ecology of the districts. Among these districts two were urban and two rural. The two urban districts were Cuttack and Khurdha which are economically advanced and near to the sea -Bay of Bengal. The geographical area of Cuttack is 3,733 square kilometers with more than 2.3 million inhabitants and Khurdha- 2,889 square kilometers with about 1.9 million inhabitants. These districts have a high population density and a high percentage of literacy. The two rural districts were Koraput and Malkangiri which are economically backward and tribal dominant. These two districts are far from

the sea with forests and hills. The geographical area of Koraput is 8,379 square kilometers with about 1.2 million inhabitants, among them about 51% are tribal. The geographical area of Malkangiri is 6,190 square kilometers with near about 0.5 million inhabitants. In these two districts literacy rate is very low, about 32% in Malkangiri and 37% in Koraput and most of the people are financially weak [50].

Participants Details

In this study three groups of health care providers were selected- medical doctors, veterinarians and drug sellers. Amongst the 24 interviewees, eight participants from each group were included. Among these eight interviewees four were from rural and four from urban districts. From each district two interviewees were included for the study from each group. Among the 24 participants only two medical doctors were female. Detail information of interviewees is summarized in Table.1.

Table.1 - Study Area and Interviewees

Interviewees	Study Area Orissa, India							
	Rural Districts				Urban Districts			
	Malkangiri		Koraput		Cuttack		Khurda Bhubaneswar	
Medical Doctors	M1	M2	M3	M4	M5	M6	M7	M8
Sex:	Female	Male	Female	Male	Male	Male	Male	Male
Age:	31 years	29 years	27 years	47 years	65 years	72 years	53 years	51 years
Qualification:	MD Com. Medicine	MBBS	MBBS	MS Surgery	MD Medicine	MS Surgery	MS Surgery	MD TB Spl.
Experience:	6 years	3 years	2 years	21 years	41 years	40 years	28 years	28 years
Interview Place:	Resident	Resident	Resident	Resident	Clinic	Clinic	Hospital	Resident
Interview Duration in minutes:	25	20	25	29	25	40	36	30
Veterinarians	V1	V2	V3	V4	V5	V6	V7	V8
Sex:	Male	Male	Male	Male	Male	Male	Male	Male
Age:	54 years	30 years	71 years	50 years	50 years	38 years	55 years	48 years
Qualification:	M.V.Sc	B.V.Sc	B.V.Sc	M.V.Sc	M.V.Sc	Poultry Mg.	M.V.Sc	B.V. Sc
Experience:	30 years	5 years	37 years	27 years	30 years	10 years	32 years	25 years
	CDVO		Retired CDVO				CDVO	
Interview Place:	Office	Hospital	Resident	Hospital	Hospital	Farm	Office	Hospital
Interview Duration in minutes:	40	20	10	21	25	20	17	15
Drug Sellers	D1	D2	D3	D4	D5	D6	D7	D8
Sex:	Male	Male	Male	Male	Male	Male	Male	Male
Age:	34 years	29 years	50 years	39 years	44 years	27 years	34 years	35 years
Qualification:	B.Pharma	B.Pharm	B.Pharm	B.Pharma	B.Pharma	B.Pharma	B.Pharma	B.Pharma
Experience:	10 years	4 years	34 years	12 years	17 years	5 years	10 years	10 years
Interview Place:	Shop	Shop	Shop	Shop	Shop	Shop	Shop	Shop
Interview Duration in minutes:	12	11	20	15	12	10	15	10

M- MBBS Doctors, V- Veterinarians and D- Drug Sellers

MBBS-Bachelor in Medicine and Bachelor in Surgery, CDVO- Chief District Veterinary Officer, M.V.Sc- Master in veterinary Surgery, B. Pharma- Bachelor in Pharmacy

Each participant was contacted by the author before the interview. Primary contact was through telephone from Sweden 15 to 20 days before interviews. Thirty six interviewees were contacted

among them 24 were considered for study to maintain the equality among study area and different group of participants.

Data collection procedure

Data were collected by face to face semi structured interview. Specific Interview guides were prepared for each group of professionals. Interviews were conducted both in local language and English. The interviews were recorded on tape and lasted approximately 20 to 25 minutes. Out of the eight medical doctors five interviews were held at their residence, two in clinic and one in the hospital. In case of veterinarians four interviews were held at hospitals, two at office and one each at residence and farm. Interviews for all the drug sellers were held at the medicine shops. All the interviews were conducted by the author who belongs to the study area, fluent in Oriya and English languages and having an educational background in Biological and Environmental Science as well as has experience in social services.

Data Analysis

The tape recorded interviews were transcribed verbatim in Oriya and then translated into English. Content analysis was applied for analysing the data. Each sentence or paragraph was coded. The tape recorded versions, Oriya and English transcripts of data were consulted time and again during coding procedure to avoid misinterpretations of the full meaning of the texts.

One of the most basic decisions when using content analysis is selecting the unit of analysis. Meaning unit was selected from the interview transcript. A meaning unit is the constellation of words or statements that relates to the same central meaning; it can be called coding unit or content unit [48]. From the meaning unit, condensed meaning unit i.e. interpretation of the underlying meaning or description close to the text was generated. A code i.e. label of meaning unit was formulated from condensed meaning unit. Similar codes were clustered together and collapsed into sub-sub categories, subcategories and categories. A category is a group of content that shares a commonality. The main themes i.e. emergent concepts were based on the similarities between categories.

Ethical Consideration

Before the interview, information was given about the purpose of the study to the interviewee, the interview guide was shown and a consent form was signed by the interviewees. The interviewee was informed that he or she can withdraw from the study at any time. All the interviews were carried out in complete privacy and the name of interviewees are confidential.

Results

Two major themes emerged from the analysis of the interviews.

´Antibiotic handling contributing to the development and spread of resistance` and ´Bi-directional relationship between antibiotic use and environment`,

The findings are presented under each major theme/category/subcategory/sub-subcategory with quotes from the respondents to illustrate the results. The results for theme-1 are presented in Table-2 and for Theme-2 in Table-3.

Table-2: Hierarchy of codes theme 1- Antibiotic "handling" contributing to the development and spread of resistance.

Theme1	Antibiotic "handling" contributing to the development and spread of resistance							
Category	"Handling" of Antibiotics				Factors influencing resistance			
Sub-category	Human use		Nonhuman use		Health system and Policy			Resistance mechanism in bacteria
Sub-sub category	Factors considered in individual prescriptions	Factors influencing prescribing	Medical uses in animals	Non medical uses in animals	Patient factors	Professional factors	Weak legislation and implementation	Drug resistance level in bacteria
Codes	Broad and Narrow spectrum High and low dose Therapeutic use Prophylactic use Choice of routes in humans "Higher" antibiotics Antibiotic combination	High density of patients Prior prescriber Variation in cost Influence of pharmacy company Unqualified medical providers Global problem	Poultry use Dairy farm Choice of routes in animals More study	Growth Promoter	Noncompliance Self-medication Ignorance Poverty Lack of awareness Patient follow up	Inadequate prescription Irrational use Improper diagnosis	Fake medicine Without prescription Low quality medicine Insufficient policy Lack of staff Erroneous posting Lack of infrastructure	Conjugation Drug tolerance Gene transfer Mutation Drug destroying Drug impermeable Multi drug resistance Cross resistance

1. Theme: Antibiotic "handling" contributing to the development and spread of resistance

Under this theme, two categories were identified (i) "Handling" of Antibiotics and (ii) Factors influencing resistance.

1.1. "Handling" of Antibiotics

Antibiotics are used both in humans and nonhumans. Under this category there are two main sub categories**:** (i) Human use and (ii) nonhuman use of antibiotics.

1.1.1. Human use

Under this subcategory two sub-subcategories are identified: (i) Factors considered in individual prescriptions and (ii) Factors influencing prescribing.

1.1.1.1. Factors considered in individual prescriptions

From this sub-subcategory mainly three concepts emerged- choice of routes, choice and uses of antibiotics.

Most of the prescribers choose the routes as per the severity of infection and disease condition of the patients. In rural area, many prescribers prefer oral route as most of the patient are living far away from the hospital, so they may not complete the injectible course. Few prescribers prescribe antibiotics for prophylactic purpose, before hospital admission of the patients, suspecting them prone to infections due to surrounding conditions.

"Prophylactic use of antibiotic means, here malaria patients are more, so when we bed admitted a malaria patient, here malaria is endemic, when we admitted malaria patients indoor, due to surrounding condition one IV[Intra venous] line is continuing, there will be chance of infection in that route, although in his blood except malaria parasite no other infection is there, there is no role of antibiotics except antimalaria, but as they are prone to infection we give antibiotic to them, that is prophylactic use (Interviewee M3)."

According to most of the prescriber`s view, broad and narrow spectrum antibiotics are classified as per the coverage of pathogens, medicine efficacy and bioavailability. Majority of them calculate dose of antibiotics according to the body weight of the patients.

"What is high and low dose, dose is calculated according to the body weight, if you do not give proper dose it is lesser amount, it is low dose, and low dose is not recover (Interviewee M5)."

Some of them think antibiotic combinations are used in mixed infections, to recover the disease immediately. Use of antibiotic combination and whether this prevents, antibiotic resistance or not is a controversy. Some of them perceive that, Pharmaceutical Company produce combination antibiotics for commercial purpose and it does not prevent antibiotic resistance. Most of them said there is a lacuna of information on whether the combination therapy reduces resistance or not.

"We do not have enough study to know either the combination therapy reduce the resistance or not (Interviewee M6)."

The term "higher Antibiotics" is used in several meaning such as- new generation antibiotics or broad spectrum or high dose of antibiotics. Some of the drug seller's say "higher antibiotics" means high cost of antibiotic. Most of them say widespread use of antibiotics is the major cause of "higher antibiotics" prescription.

1.1.1.2. Factors influencing prescribing

Major inferences emerging under factors influencing prescribing are- high patient density, prior prescription by unqualified prescribers, medicine cost and influence of Pharmaceutical Company on the prescribers.

As per almost all interviewees' observation, patient density is high in both rural and urban area hospitals. One doctor prescribes approximately fifty to ninety patients per day. The majority of them said that high patient density affects antibiotic prescription; it may cause improper diagnosis hence inappropriate treatment and misuse of medicine.

"We are always doing improper diagnosis due to high density of patients (Interviewee M6)."

"When one doctor comes early morning, he is mentally free, huge number of patients are coming, he is treating one by one. When many patients gather around him, at a time five person are speaking, five types of things, he will loose his concentration, he cannot answer to anyone perfectly, he cannot satisfy to a single patient, maximum we have to see twenty to twenty one, but what will we do? (Interviewee M7)."

All medical doctors mentioned that before visiting an authorised medical consultant maximum patients are taking early treatment from quack [An untrained person who pretends to be a physician and dispenses medical advice and treatment]- unauthorised unqualified medicine practitioner or directly taking from the medicine shop with the reference of drug sellers or by their diminutive knowledge.

According to the opinion of many, quacks are prescribing incomplete course and dose of antibiotics. They are using antibiotics empirically. Few of the prescribers also suggested training of quacks for prudent drug use and authorising them for prescribing, since there is a sacristy of authorised medical practitioners compared to the requirement.

"Usually in this Malkangiri, tribal area RMP [Registered Medical Practitioner, a type of diploma holder for medicine from early days] or quacks are the primary prescribers (Interviewee M1)."

According to many interviewees cost and effectiveness of antibiotics vary among different companies. Some of them say sometimes some prescribers are influenced by a particular company and prefer to prescribe their medicines.

"Now a day's all are searching some income source [some of the prescribers are influenced by specific company]. A number of Pharmacy Companies are coming with Ajaba (strange) combinations. Although some antibiotics do not lose their favours, doctors are not prescribing them (Interviewee M2)."

"In my view those who are good physician, no pharmacy company influence them, we will not compromise with life saving drug, if small company provide crore crore rupees [huge amount of money] I will never prescribe their medicine (Interviewee M8)."

1.1.2. Nonhuman use

Antibiotics are the drugs which are used not only in human treatment but also treatment of animals. Under this subcategory two sub-subcategories emerged: (i) Medical uses in animals and (ii) Non medical uses in animals.

1.1.2.1. Medical uses in animals

Antibiotics are most commonly used in diary farm, pet animals and poultry farm for therapeutic purpose in animals. All most all veterinarians prefer intramuscular routes in animals. As per the view of poultry prescribers, oral dose with water is suitable route in birds. As per the veterinarian's version, antibiotics which are used in humans, same antibiotics are used in animals such as penicillin, amoxicilin, coxacilin, ciprofloxacilin and tetracycline.

"Which antibiotic we use in veterinary, same antibiotic is used in humans; there is no difference in veterinary Aushadha (medicine) and human medicine (Interviewee V4)."

"Generally tetracycline and oxytetracycline is used in poultry (Interviewee V5)."

Some interviewee's opinion was that when antibiotics are used in diary farm during lactation, it may affect the humans, but more study is required to understand the phenomenon behind it.

"During lactation period, which antibiotic will reliable that will impact. Drug dose, drug availability, drug excretion, how much available in tissue, what is the secretion rate, if we are not know this we cannot say it is impact or not, if drug is not excreted it is deposited. (Interviewee M4)."

"If there will be chance of passing antibiotic in breast milk, why not in cow milk. It may pass antibiotic (Interviewee M1)."

1.1.2.2. Non medical uses in animals

The most common non medical use of antibiotics in animals is as growth promoters in feeds. All most all prescribers dislike prescribing antibiotics as growth promoters. Few of them also advocate using probiotics, instead of antibiotics in animal feed.

"In poultry antibiotics are use as growth promoter, mixing antibiotics in feed (Interviewee V5)."

1.2. Factors influencing resistance

Under this category there are two main sub categories: (i) Health system and policy and (ii) Resistance mechanism in bacteria.

1.2.1. Health system and policy

Health system and policy are two opposite sides of a single coin. It is exigent, multipart and dynamic in nature. It depends upon the various factors such as patient, professional and legislative.

Under this subcategory emerged sub-subcategories are: (i).Patient factors, (ii).Professional factors, and (iii).Weak legislation and implementation.

1.2.1.1. Patient factors

According to most of the interviewees' patients' noncompliance nature, self medication, ignorance, poverty, lack of awareness and irregular follow up are the possible causes of drug resistance.

Most of the prescribers thought that patient's noncompliance nature such as incomplete course, irregular course, negligence and overconfidence in antibiotic uses cause improper use and resistance to antibiotics. Sometimes patient doesn't follow the prescriber`s instruction for apposite use of medicine. Patients do not have awareness for appropriate use of antibiotics. Most of the patients are ignorant about the antibiotic and its proper use. They are not aware about the prospect of improper use of antibiotics.

"If we prescribe antibiotics to a patient for 7days, if he feels cure in 3days, he discontinues the course, he is not taking complete course, in that case he is symptomatically relief, but bacteria are not kill, that bacteria develop resistance (Interviewee M7)."

Many of the prescribers say poverty and self-medication are two major reasons for incomplete course of antibiotics. Due to high cost of antibiotics some patients are unable to purchase full course of medicine.

"Some patients not able to purchase the complete course due to their bad financial condition, they took only 2-3 days. As it is rural area financial condition is most important (Interviewee M2)."

As per all most all prescribers view, incomplete course due to poverty is more common in rural area and due to self-medication in urban area. In urban area educated patients with little knowledge of medicine prefer to purchase incomplete course from the medicine shop.

"We get more prescription or some people also directly telling the name of the medicine also. Those have little bit knowledge they are taking two or three tablets without prescription. They are not taking full, only two or three. They say, they will take (Interviewee D4)."

1.2.1.2. Professional factors

The majority of the prescribers believe inadequate prescription, irrational use of antibiotics and improper diagnosis of diseases are the major professional factors which are responsible for misuse of antibiotics. As per their concept, inadequate prescription means inadequate dose, poor or short dose, which is not sufficient to meet the need and too short duration of course. Irrational use involves wide spread, indiscriminant, improper, random, haphazard use of antibiotics and improper treatment of diseases. In some cases without proper diagnosis of disease, antibiotic are used. This erroneous way of antibiotic treatment at professional level is responsible for antibiotic resistance.

"Here in Cuttack also doctor are not available, quacks are treating, they are switch over to higher antibiotics, what they thought that I gave low to high, they have some idea, they help to the society, but they have no idea about the dose (Interviewee M6)."

Some of the prescribers used antibiotics in common cold although they know that, it is a viral infection for suspecting secondary bacterial infection.

"Frankly I am speaking here we are not giving antiviral. Common cold is a viral disease, few people know this, but still we are using antibiotic for this, because due to viral infection, there will be chance of secondary infection, to prevent this we are giving antibacterial, not for original viral infection (Interviewee M3)."

"Sometimes our doctors also doing mistreatment, which medicine is not required they are sometimes prescribing that, without completing one course switch over to another one, if you have a reason you change it. (Interviewee M4)."

Many of the veterinarians said due to lack of infrastructure they are using antibiotics empirically.

"In our veterinary field we are using antibiotics randomly, if you compare our system with human or medical side, it is not systematised, laboratory is not so developed, that's why without culture sensitive test we are doing treatment (Interviewee V7)."

1.2.1.3. Weak legislation and implementation

Most of the interviewee's opinion was that weak legislation and implementation of health system is responsible for antibiotic resistance. Due to weak drug policy, fake and low quality medicine is available. Antibiotics are available in medicine shop without doctor's prescription.

"Now in India Nakali Aushadha (fake medicine) also available, I do not know how it is possible (Interviewee M8)."

"It is very difficult to know the quality of Aushadha (medicine). Nowadays all the medicines cover packed are excellent, but it sometimes contain worst medicine. It will melt and damage (Interviewee M1)."

Most of them suggested that there is need of strong drug policy to improve the rational use of drug. They suggested that selling of drug without authorized medical prescribers' prescription should be banned. Most of the doctors suggested that medicine which is used in humans should not be used in animal treatment.

"Some drug control policy is essential, we have no such type of strict policy, here without prescription we can get everything, you go developed country you cannot purchase any drug without prescription that is needed here, and there must be some selling rule especially for antibiotics (Interviewee M4)."

"Unauthorised medicine practice should be banned, either they are quacks or homeopathic or aurivedic doctors, they should write their medicine. If you go to field side, you will see majority of them are prescribing antibiotics, they do not know the dose. Our drug is like OTC products, half of the drug which is banned in developed country; it is a dumping ground, which is banned there, that is deposited here (Interviewee M4)."

"In India for commercial purpose, they are not following scientific things, everything commercial. Now medicine seller also half doctor, he does not have idea about dose , course he is prescribing medicine, for them hard and first rule is required because they are selling a life saving drug like Machha sukhua (fish and dry fish) (Interviewee M8)."

Some of them said lack of medical staff in hospital; erroneous posting of doctors and lack of infrastructure for medical care are the indications of reprehensible health management system.

"In allopathic post Auruvedic doctors are there, they do not have more knowledge about antibiotic, but they are prescribing antibiotics. They study ayurvedic and prescribing allopathic; how far is it correct (Interviewee D4)."

Some of the interviewees said that there is a lack of good laboratories for culture sensitive test of the organisms, which cause improper diagnosis, hence irrational use of antibiotics. It is very difficult to know the quality of the drugs.

"There are no advanced tools to evaluate the quality of the medicine; there is no tool and technique (Interviewee M4)."

"In our veterinary field laboratory is not so developed, that's why without culture sensitive test we are doing treatment (Interviewee V7)."

1.2.2. Resistance mechanism in bacteria

Abuse of antibiotic handling causes resistance to specific antibiotic in bacterial level.

1.2.2.1. Drug resistance level in bacteria

Some of practitioners said that if once one bacterium is resistant to a particular antibiotic, it transfers resistance gene either by conjugation or transformation. Gene mutation occurs in the genetic level to adapt to specific antibiotic. The most important characteristics of resistant bacteria are drug tolerance, drug destroying and drug impermeability. Multi drug resistance and cross resistance are the pressing problems at the bacterial level.

"Patient is not taking complete course, in that case he is symptomatically relief, but bacteria are not kill, that bacteria develop resistance, what does not kill them makes them stronger (Interviewee M7)."

2. Theme 2: Bi-directional relationship between antibiotic use and Environment

Under this theme, two categories are identified: (i) Influence of eco factors on antibiotic prescription and (ii) Influence of antibiotic use on Environment (Table 3).

Table-3: Hierarchy of codes theme 2- Bi-directional relationship between antibiotic use and Environment.

Theme2	Bi-directional relationship between antibiotic use and Environment			
Category	Influence of eco factors on antibiotic prescription		Influence of antibiotic use on Environment	
Sub Category	Abiotic factors	Biotic factors	Effect of antibiotics on surroundings	Effect of antibiotics on organisms
Codes	Coastal area Seasons High temperature Pollution	Forest area Population density	Water Terrain Air	Micro organisms Aquatic organisms Grazing animals Rural people

2.1. Influence of eco factors on antibiotic prescription

Environmental factors have significant impact on antibiotic prescription. These factors may be nonliving or living in nature. Under this category there are two main sub categories**:** (i) Abiotic factors (ii) Biotic factors.

2.1.1. Abiotic factors

Abiotic factors are the nonliving components of an ecosystem. It may be physiographic factors or climatic factors.

As per the interviewees perception the most important physiographic factors which influence the antibiotic prescription are geographical location of the area such as costal or hilly area. Some of them view that in coastal area people are rich; they are using higher antibiotics. In hilly area most of the patients are tribal and poor, they prefer traditional treatment, they have not enough money to use modern treatment or they are not taking complete course of antibiotics.

"In my view rampant use of antibiotics is one cause of resistance, that is not here [Koraput, hilly area] more, that is more in costal belt, because I have seen; in coastal area for a normal infection they are prescribing higher antibiotics. In coastal area for minor infection, they are giving higher antibiotics (Interviewee M3)."

According to most of interviewees the climatic factors such as seasons, temperature and pollution have significant impact on antibiotic prescription. In summer season due to high temperature, there is more stress and hence more diseases, so in summer, antibiotic prescription is higher. In winter, due to cold, respiratory tract infections and in rainy season, diarrhoea are more common.

"According to season's diseases, according to diseases treatment or medicine, loose motions, during rainy season, and then we will prescribe randomly ofloxacin, metronidazole during rainy season (Interviewee M2)."

Some of the prescribers' perception is that pollution has significant impact on antibiotic prescription. In industrial area lung infection is more common. Due to pollution, respiratory diseases are increasing. In polluted area resistant bacteria spreads quickly.

"If pollution is more antibiotic resistant is quickly. In crowded and industrial area asthma is common. In hygienic condition asthma is less. Where pollution is more lung infection is more. Now higher antibiotic are used. What I said if in pollution area antibiotic are used for long day. We have to change two or three antibiotics (Interviewee M1)."

"In polluted air resistance bacteria are there, in conjugation they will transfer resistance gene to other non-resistance bacteria, if pollution is more resistance factor are spreading quickly (Interviewee M6)."

2.1.2. Biotic factors

Biotic factors are the living factors in the environment i.e. plants, animals and micro organisms. In forest area generally, tribal and poor people are living. As per the findings of this study, in this area population density is less but patient's density is high in hospital due to not as much of hospitals.

Some of the interviewees viewed incomplete course is more common in tribal or hilly area. They thought this happened due to bad financial condition as patients are unable to purchase complete course of medicine.

High population density also affects antibiotic prescription. Due to high population density and fewer health care facilities, patient density is high in hospital which causes improper diagnosis and misuse of antibiotic treatment.

"Due to over crowd infectious diseases is more common, if population density is more, then more disease and then more antibiotics (Interviewee M5)."

2.2. Influence of antibiotic use on Environment

Improper disposal of antibiotics contaminates the environment. It affects the organisms also. It may be one of the possible reasons of antibiotic resistance. Under this category two main sub categories emerged**:** (i) Effect of antibiotics on surroundings and (ii) Effect of antibiotics on organisms.

2.2.1. Effect of antibiotics on surroundings

Most of the interviewees suggested that due to improper disposal of pharmaceuticals, now antibiotics are found in air, water and terrain. It contaminates lentic (stagnant or still water) and lotic (actively moving water) water as well as wetlands.

"We are doing operation [surgical treatment], after cutting we throw it in to drain water, it mix with river water, and it contaminate the water (Interviewee M6)."

"If we are not disposed expired medicine properly, we throw it outside it will impact on resistance, that will degrade in atmospheric air and sunlight and mix with air, we inhale it and taking the medicine in indirect way to our body, that time we have some infection, we take that in improper way, it will effect to the body (Interviewee M8)."

Most of the veterinarians viewed that when pharmaceuticals are thrown on the terrain, it is dangerous for grazing animals.

"Medical waste contains antibiotics; this is a serious problem for veterinary. When we throw medical waste outside, these are taken by grazing animals, we are throwing outside; animals are taking this during grazing (Interviewee V8)."

As per their knowledge there is not much study in this area, further research is required in order to find out the exact problem and its solution.

"Antibiotics resistance in relation to environment is a research question (Interviewee V4)."

2.2.2. Effect of antibiotics on organisms

Some of the interviewees said that when antibiotics are disposed improperly it affects micro organisms, aquatic organisms, grazing animals and rural people that are using river or pond water for drinking and cooking.

"If disposal medicine mix with water and that water is taken by cows, buffalos or rural people use it for drinking purpose, it will impact on them (InterviewеeV8)."

"Expired medicine if thrown outside, it will impact on environment, when it will mix with water that water is taken by rural people it will surely impact. What we waste if it will indirectly use again it will create problem, we throw it, it will mix with water, again we drink that water that water again went into blood, and obviously it will impact (Interviewee M7)."

Some of the interviewees assumed that antibiotics in environment have significant impact on ecology of organisms, as it may cause resistance in water borne pathogenic bacteria, when they are exposed to concentration levels of antibiotics in water and also it may cause resistance, when antibiotic contaminated water goes in intake of animals or humans. According to their perception more study is required to understand this complex phenomenon.

"When ever the water borne diseases bacteria create slow dose of antibiotic everyday, they gradually tolerant to that particular drug and develop resistance (Interviewee V6)."

"Now you are normal man, if antibiotic will given to you it must impact, so if expired medicine will mix with water and that water is taken by cows, sheep or human it must impact, there is no doubt. But intense study is required on this area (Interviewee V4).

Discussion

To my knowledge, this is the first qualitative study in Orissa, India, on the views of medical doctors, veterinarians and drug sellers, on uses of antibiotics and its impact on environment. The main finding of the study was, mishandling and abuse of antibiotics in patients as well as at professional level due to weak implementation of legislation appears to be the major cause of development of resistance to antibacterial agents. In this study it was observed that patients' noncompliance nature and self-medication are the imperative factors of antibiotic resistance. Incomplete course or dose due to poverty in rural area and self medication in urban area are more common. Lack of infrastructure and high patient density are the possible causes of improper diagnosis and hence irrational use of antibiotic by the trained medical doctors. Quacks or untrained medical practitioners are using antibiotics inadequately and improperly which is the major cause of resistance. It was also found that the antibiotics which are used for human treatment, same antibiotics are used in veterinary and as growth promoter in poultry. As per the interviewees view due to insufficient drug policy and implication, fake or counterfeit drugs and antibiotics without prescription are available in medicine shops. These are the possible causes of misuse and consequently resistance of bacteria to antibiotics. Apart from the misuse of antibiotics at professionals and patients level, the study also explored that climatic factors, pollution and population density are the major ecological factors which influence antibiotic prescriptions. Another major finding of this study was due to improper disposal system of pharmaceuticals; antibiotics are contaminating air, water and terrains, which can cause major risk to aquatic and grazing animals.

Noncompliance is a serious problem in clinical practice. In this study it was found that patients' noncompliance nature such as incomplete course, irregular course, negligence and overconfidence is the major cause of improper use of antibiotics, which is one of the possible reasons for antibiotic resistance in patient's level. Self-medication and poverty is the key factor for incomplete course. Incomplete course due to self-medication in urban areas and due to poverty in rural areas is more common. A previous study in Europe showed that public attitudes, beliefs and knowledge concerning antibiotic use, self medication and antibiotic resistance are varying among different patients and awareness about antibiotic resistance was the lowest in countries with higher prevalence of resistance [19]. Self-medicated patients used inadequate drugs or dose [20]. Similar study on self-medication in Latin America showed that, patients believe that visit to physician for a diagnosis and prescription were unnecessary, when the patient was familiar with the symptoms and he had previously responded to antibiotic treatment [21]. In Trinidad and Tobago, it was found that inappropriate use of antibiotics resulted from self-medication [22]. In rural areas patients are financially weak; they do not have enough money to purchase the full course of prescribed medicine. Typically, in developing countries complex socioeconomic and behavioral factors are associated with antibiotic resistance [24]. Our results also indicate that public knowledge and awareness on prudent use of antibiotics is diminutive.

The results showed that the most common cause of antibiotic abuse at professional level is because of lack of infrastructure, inadequate prescription and irrational prescription by unauthorised as well as authorised health prescribers or dispensers. Most of the prescibers informed that there is a lack of laboratory for culture sensitivity test, due to this reason they are improperly diagnosing the disease and then prescribe antibiotics symptomatically which may cause

irrational prescription. According to all most all doctors' perception, quacks or unauthorised medical prescribers are prescribing antibiotics improperly; they do not have adequate knowledge on dose and course of antibiotics. They are not providing complete course, which is inadequate prescription. It is one of the possible causes of antibacterial agent resistance. Few of the interviewees suggested training of quacks on prudent use of antibiotics and authorising them for prescribing medicine, because in Orissa, there is a lack of certified or trained doctors as per the requirement and they are saving the life of patients in remote areas where availability of trained prescriber is not at all or less. Some of the prescribers are using antibiotics in common cold, a viral disease for suspecting secondary bacterial infection. Similar study showed that both in France and Britain about 90% of the patients receive antibiotics for tonsillopharyngitis [26]. As per a previous study, understanding of distinction between virus and bacterium often led to perceived confusion [25]. There is a misuse of antibiotics by health professionals, unskilled practitioners, and laypersons; poor drug quality; unhygienic conditions are accounting for spread of resistant bacteria; and also inadequate surveillance [24]. Irrational prescribing habits of clinicians are an important reason for unreasonable prescription of drugs in clinical practice [17].

Legislation and its implementation are the key elements to control abuse of drugs. As maintained by the interviewees due to weak legislation and its weak implementation, low quality medicine and fake or counterfeit drugs are available. As per a previous study in India, it was estimated that 15-20% of all drugs were counterfeit and substandard [45]. Counterfeit drugs often contain the wrong ingredient, contain no active ingredient, or contain only weak and inadequate amounts of the active ingredients; medicine manufactured below established standards of quality and therefore dangerous to patients' health and ineffective for the treatment of diseases [13,46]. India's pharmaceutical companies have suggested that in India's major cities, one in five medicines sold was a fake. Counterfeit drugs are not only sold in countries with ineffective drug regulation but they are also exported or re-exported. The regular use of substandard or counterfeit medicines can lead to therapeutic failure or drug resistance [46].

In this study it was also found that antibiotics are purchased without prescription from the medicine shops. A previous study in Kerala, India, found that 20% of the antibiotics are purchased without doctor's prescription; however a cross sectional study in Zimbabwe showed that, there is a low sale of antibiotics without prescription which is in sharp contrast to other studies from low income countries [32]. Non-prescribed use of antibiotics is very low in Sweden compared with other European countries [33]. Similar study from nine African countries suggest that, since most people purchase their drugs from unqualified drug sellers, educating these drug sellers would probably be more beneficial for public health in many low-income countries [31].

In this study, it was observed that antibiotics are empirically used in veterinary due to lack of laboratory facilities for culture sensitivity test. Another antibiotic use in veterinary is as growth promoter in poultry feeds. The antibiotics generally used in animals are penicillin, amoxicillin, coxacilin, ciprofloxacilin, and tetracycline. Due to lack of supervision of Government in poultry farm, the farmers are using indiscriminately antibiotics in feeds which are the foremost problem for environmental pollution due to antibiotics as well as resistance of antimicrobial agents. According to WHO report, some newly emerging resistant bacteria in animals are transmitted to human; mainly via meat and other foods of animal origin or through direct contact with farm

animals [5]. Veterinary prescription of antimicrobials also contributes to the problem of resistance [2].

Due to improper dose of antibiotics, pathogenic bacteria adapt to particular drugs at genetic level and transfer the resistant gene information to other nonresistant bacteria. That's why antibiotic resistance is a pressing public health problem.

An important finding of this study was the influence of ecological factors on antibiotic prescription. All most all interviewees said that antibiotic prescription varies according to geographical location of the area, population density, seasons, temperature and pollution rate. In coastal area generally prescribers prefer to prescribe "higher antibiotics". In high population density and more polluted area resistant strains spread quickly, hence in this area there is a high prescription of antibiotics. High temperature causes more stress, hence more diseases, so antibiotic prescription is higher in summer. In winter respiratory tract infection and in rainy season diarrhoea are more common.

Another major finding of this study was the environmental impact of antibiotics. As per most of the interviewees, the main environmental pathway of antibiotics is from pharmaceutical use and it has significant ecological as well as public health impact. The sources are disposal of containers and unused medicine, human consumption, aquaculture and companion animals. This contaminates the terrain as well as aquatic environment. It may be one of the possible reasons for the resistance to antibiotics in water born bacteria, due to exposure to below threshold concentration of antibiotic in water. As per a study in Spain, it was found that *Enterobacteriaceae* and *Aeromonas* spp. fresh water bacteria are resistant to nalidixic acid, quinolones and tetracycline due to mixing of urban effluent in fresh water [44]. According to a study in Patancheru, which is a major production site of the generic drugs for the world market, near Hyderabad, India, high levels of several broad spectrum antibiotics specifically ciprofloxacin were presents in aquatic environment [10]. A degree of multiple antibiotic resistances was observed in seven different *Vibro* species in the coastal water of Bay of Bengal at Orissa coast [41]. Antibiotics have been detected in surface water in many countries such as Canada, Germany, United States and other European countries [42]. A study in Germany showed that in surface water out of fourteen pharmaceuticals, 30% are antibiotics [12]. A study in Australia mentions presence of three antibiotics i.e. ciprofloxacin, norfloxacin and cephalexin both in sewage effluent and environmental waters downstream from a sewage discharge [11]. A wide range of pharmaceuticals has been found in fresh and marine waters, and it has recently been shown that even in small quantities, some of these compounds have the potential to cause harm to the aquatic life. Only little is known about occurrence, fate, effect and risk of antibiotics in the environment. It is important to know the amounts of antibiotics released in the aquatic environment to be able to properly evaluate the risks, effect and potential impacts of these products.

Methodological Consideration

In order to improve the trustworthiness of this study, data triangulation method was used during data analysis. Data was collected from different health professionals including medical doctors, veterinarians and drug sellers. The informants varied in geographical and socioeconomic area, in this case rural and urban area. During coding procedure to avoid misinterpretation of the

full meaning of the text, both Oriya and English version of transcripts and also in some complex case, tape recorded data were used simultaneously. In the analyses, this discernment served to broaden the interpretation and final result is the negotiated outcome of this. In this study female participants are limited. So we can not differentiate the antibiotic prescription variation of male and female practitioners. But in India, in underdeveloped regions like Orissa, female medical practitioners are relatively less, so this was not intentional on our part. Apart from this, other nonhuman antibiotic uses like aquaculture, agriculture and horticulture are also not considered in this study. Further studies are required in order to develop deeper understanding of this complex phenomenon.

Policy Implication

Antibiotic use is influenced by the knowledge and prospect of prescribers as well as patients, economic incentives, country's health system, and the regulatory environment. Research programmes alone are dubious to improve antibiotic use. Priority programme actives would include a cautiously planned combine activity by Governments, health training institutions, health delivery systems, pharmaceutical companies, prescribers, consumers and international organisations. Surveillance required at all levels in order to obtain an accurate picture of emerging resistances and the rate of transmission of new resistances. Both national and local efforts will be required for prudent use of antibiotics. Orissa has adopted Central government guidelines, policies and programmes for the health care development. In the recent years, there have been a number of statewide initiatives to enhance the quality of the health care system to improve the health of the people; distribution and rational use of drugs is one of the initiatives among them [49]. The need for promoting appropriate use of drugs in health care system is a big concern, but also there is a need for supervision for making the existing laws to ensure rational sale and use of antibiotics. It is required to ban the sale of antibiotics without prescriptions. To use antibiotics more judiciously in hospitals, intensive teaching of the principles of prudent use of antibiotics is essential. There is need of pre-campaign surveys to assess baseline knowledge, attitudes, and behaviour among public and professionals about antibiotics use, resistance problem and environmental impact of pharmaceuticals. Most often high antibiotics are prescribed for infections caused by viruses that are obviously unresponsive to antibiotic therapy. There is also need to review the antibiotic prescription practices of the clinicians. Quality control of drugs, action against pharmaceutical companies who produced low quality or counterfeit drugs and modernized laboratory facility for proper diagnosis of diseases is essential to overcome this foremost public health crisis. Antibiotics should not be used as growth promoters, control of nonhuman use of antibiotics and banning of use of the antibiotics which are used in human medicine in animals is necessary. There is also need of public awareness programme for appropriate use and disposal of pharmaceutical products to protect our environment from pharmaceutical wastes and prudent use of life saving drugs.

Further Research

Environmental risk from antibiotics remains largely unknown. In spite of recent investigation on information about pharmaceuticals in the environment, important information on their fate and long term effect is still lacking. The knowledge on source and fate of antibiotics and their metabolites in the environment is important to estimate their potential impacts on ecology and human health. Hence further research is required to identify the factors that influence the wide

range of antibiotics in the environment and its role on antibacterial resistance as well as toxic effect to terrain and aquatic organisms. There is no scientific publication on influence of ecological factors on antibiotic prescriptions so more study is essential in this field. As use of combined antibiotics therapy is increasing tremendously further study is also essential to determine whether combination therapy has reduced antibiotic resistance or not.

Conclusion and recommendations

Antibiotic resistance is a serious public health concern with economic, social and political implications. This study emphasises the need for comprehensive actions including information, training, legislation and education at all levels of drug delivery system to rationalize antibiotic use by improving prescribing pattern and creating awareness among consumers. This study recommends following preventive measures for prudent use of antibiotics. Antibiotics should not be used as growth promoters in animals and certain antibiotics should be used only for human medicine. All antibiotics should be sold only by prescription of autherised medical practitioners and availability of quality drug at affordable costs should be ensured. Proper diagnosis of diseases, timely and accurate reporting of microbial susceptibility test results for selection of appropriate antibiotics and focused therapy which helps to reduced inappropriate use of broad spectrum antibiotics is essential. Proper disposal of pharmaceutical wastes is required to prevent the contamination of environment from pharmaceutical pollutants. The knowledge on persistent pharmaceuticals in soil and water is limited. Further research is required concerning impact of antibiotics on natural microbial communities in the environment.

References

1. WHO. World Health Report 2003. Shaping the future.
2. WHO. WHO fact sheet No 194, January 2002. Antimicrobial resistance.
3. International Workshop on Antibiotic Resistance: Global Policies and Options, 28 February 2000, Center for International development, Harvard University.
4. Kapil A. The challenge of antibiotic resistance: Need to contemplate. Indian J Med Res 2005; 121: 83-91.
5. WHO.WHO fact sheet NO. 268, January 2002. Use of antimicrobials outside human medicine and resultant antimicrobial resistance in humans.
6. Okeke IN, Laxminarayan R, Bhutta ZA, Duse AG, Jenkins P. O'Brieen TF, Pablos-Mendez A, Klaigman KP. Antimicrobial resistance in developing countries. Part 1: Recent trends and current status. Lancet Infect Dis. 2005; 5: 481-93.
7. Ungemach FR, Muller-Bahrdt D, Abraham G. Guidelines for prudent use of antimicrobials and their implications on antibiotic usage in veterinary medicine. Int J Med Microbiol 2006; 296: 33-8.
8. Jones OA, Voulvoulis N, Lester JN. Potential impact of pharmaceuticals on environmental health. Bull World Health Organ 2003; 81: 768-9.
9. A world first: European research discovers solutions to environmental impact of antibiotics Brussels June 2003.
10. Larsson DG, de Pedro C, Paxeus N. Effluent from drug manufactures contains extremely high levels of pharmaceuticals. J Hazard Mater 2007; 148: 751-5.
11. Costanzo SD, Murby, Bates J. Ecosystem response to antibiotics entering the aquatic environment. Mar Pollut Bull 2005; 51: 218-23.

12. Schlusener MP, Loffler D, Ternes TA. Knowledge and need assessment on pharmaceutical products in environmental waters. Sixth Framework Programme July 2008.
13. WHO. Overcoming Microbial Resistance. Infectious Disease Report 2000.
14. Malhotra P, Lofgren H. India's pharmaceutical industry: hype or high tech take- off? Aust Health Rev 2004; 28: 182-93.
15. Dahlgren L, Emmelin M, Winkvist A. Qualitative methodology for International public health. Umeå University 2007 pp 2.
16. Lakshmi V. Need for national/regional guidelines and policies in India to combat antibiotic resistance. Indian J Med Microbiol. 2008; 26:105-7.
17. Sharma R, Sharma CL, Kapoor B. Antibacterial resistance: current problem and possible solutions. Indian J Med Sci. 2005; 59:120-9.
18. Dineshkumar B, Raghuram TC, Radhaiah G, Krishnaswamy K. Profile of drug use in urban and rural India. Pharmacoeconomics 1995; 7: 332-46.
19. Grigoryan L, Burgerhof JG, Degener JE, Deschepper R, Lundborg CS, Monnet DL, Scicluna EA, Birkin J, Haaijer-Ruskamp FM:SAR consortium. Attitudes, beliefs and knowledge concerning antibiotic use and self-medication: a comparative European study. Pharmacoepidemiol Drug Saf. 2007; 16:1234-43.
20. Bojalil R, Calva JJ. Antibiotic misuse in diarrhea. A household survey in a Mexican community. J Clin Epidemiol 1994; 47:147-56.
21. Mainous AG 3rd, Diaz VA, Carnemolla M. Factors affecting Latino adults' use of antibiotics for self-medication. J Am Board Fam Med. 2008; 21:128-134.
22. Parimi N, Pinto Pereira LM, Prabhakar P. The general public's perceptions and use of antimicrobials in Trinidad and Tobago. Rev Panam Salud Publica. 2002; 12: 11-8.
23. Gnanou JC, Sanders P. Antibiotic resistance in bacteria of animal origin: methods in use to monitor resistance in EU countries. Int J Antimicrob Agents. 2000; 15: 311-22.
24. Okeke IN, Lamikanra A, Edelman R. Socioeconomic and behavioral factors leading to acquired bacterial resistance to antibiotics in developing countries. Emerg Infect Dis. 1999; 5: 18-27.
25. Butler CC, Rollnick S, Pill R, Maggs-Rapport F, Stott N. Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throats. BMJ 1998; 317: 637-42.
26. Carbon C, Bax RP. Regulating the use of antibiotics in the community. BMJ 1998; 317: 663-5.
27. Sivagnanam G, Thirumalaikolundusubramanian P, Mohanasundaram J, Raaj AA, Namasivayam K, Rajaram S. A survey on current attitude of practicing physicians upon usage of antimicrobial agents in southern part of India. MedGenMed. 2004; 6:1.
28. Saradamma RD, Higginbotham N, Nichter M. Social factors influencing the acquisition of antibiotics without prescription in Kerala State, south India. Soc Sci Med. 2000; 50: 891-903.
29. Sosa A, Travers K. Physician Antibiotic Prescribing Practices and Knowledge in Seven Countries in Latin America and the Caribbean. A PAHO/APUA Report 2002.
30. Kuzujanakis M, Klienman K, Rifas-Shiman S, Finkelstein JA. Correlates of parental antibiotic knowledge, demand, and reported use. Ambul Pediatr. 2003; 3: 203-10.
31. Viberg N, Tomson G, Mujinja P, Lundborg CS. The role of pharmacist-voices from nine African countries. Pharm World Sci 2007; 29: 25-33.
32. Nyazema N, Viberg N, Khoza S, Vyas S, Kumaranayake L, Tomson G, Lundborg CS. Low sale of antibiotics without prescription: a cross-sectional study in Zimbabwean private pharmacies. J Antimicrob Chemother 2007; 59: 718-26.

33. Grigoryan L, Haaijer-Ruskamp F, Burgerhof JG et. al., Self-medication with antimicrobial drugs in Europe. Emerg Infect Dis 2006; 12: 452-9.
34. Lathers CM. Role of veterinary medicine in public health: antibiotic use in food animals and humans and the effect on evolution of antibacterial resistance. J Clin Pharmacol 2001; 41:595-9.
35. Wegener HC. Risk management for the limitation of antibiotic resistance-experience of Denmark. Int J Med Microbiol. 2006; 296: 11-13.
36. Mason IS, Kietzmamnn M. Cephalosporins-pharmacological basis of clinical use in veterinary dermatology. Veterinary Dermatology 1999; 10: 187-92.
37. Wise R, Hart T, Cars O, Streulens M, Helmuth R, Houvinen P, Sprenger M. Antimicrobial Resistance. Is a major threat to public health. BMJ 1998; 317: 609-10.
38. Grave K, Greko C, Nilsson L, Odensvik K, Mork T, Ronning M. The usage of veterinary antibacterial drugs for mastitis in cattle in Norway and Sweden during 1990-1997. Prev Vet Med. 1999; 42: 45-55.
39. Tollefson L, Flynn WT. Impact of antimicrobial resistance on regulatory Policies in veterinary medicine: status report. AAPS PharmSci 2002; 4:E37.
40. Bound JP, Voulvoulis N. Household disposal of pharmaceuticals as a pathway for aquatic contamination in the United Kingdom. Environ Health Perspect 2005; 113: 1705-11.
41. Dash SK, Rath CC, Ray P, Adhikary SP. Effects of antibiotics and some essential oils on marine Vibrios isolated from the coastal water of Bay of Bengal at Orissa coast. Journal of Pure & Applied Microbiol. 2007; 1:247-50.
42. Yargeau V, Leclair C. Impact of operating conditions on decomposition of antibiotics during ozonation: a review. Ozone: Science and Engineering 2008; 30: 175-88.
43. Kummerer K. Significance of antibiotics in the environment. J Antimicrob Chemother 2003; 52: 5-7.
44. Laing R, Hogerzeil H, Ross-Degnan D. Ten recommendations to improve use of medicines in developing countries. Health Policy Plan. 2001; 16:13-20.
45. Chaudhury RR, Parameswar R, Gupta U, Sharma S, Tekur U, Bapna JS. Quality medicines for the poor: experiences of Delhi programme on rational use of drugs. Health Policy and Plan 2005; 20:124-36.
46. WHO. WHO fact sheet No 275, November 2006. Counterfeit medicines.
47. Hsieh HF, Shannon SE. Three Approaches to Qualitative content Analysis. Qualitative Health Research 2005; 15: 1277-88.
48. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Education Today 2004; 24:105-12.
49. Orissa State integrated Health Policy-2002.
50. http://www.123orissa.com/exploreorissa/distinfo/default.asp

Appendices

Appendix: Interview Questionnaires

SET –A

MBBS Doctors

Name: Place:
Profession: Interview Date:
Office Address: Starting Time:
Ending Time:

Age:
Sex:
Experience:

A. Knowledge and Practice in Prescribing Antibiotics

Introductory questions	**Probing Area questions**
Patient encounter	
1. How many patients do you see in a day?	-Rationality
2. How many patients need antibiotics?	
3. How you choose antibiotics while prescribing?	-What infectious diseases encounter? - Bacterial, Viral and others
4. Can you share with me the common antibiotics that you use in your locality?	-Name of antibiotics, brands. -Route -Dose, Course - Prophylactic and therapeutic uses.
5. How you treat the patient who is treated earlier?	- Do you get patients in your OPD with prior use of antibiotics? - Who were the prior prescribers? - What antibiotics they prescribing? (RTI, diarrhea, common cold etcs) - Are you sure your patients take full course of antibiotics?
6. What is your view on socioeconomic status of patients and antibiotic use?	- Does the cost factor play any role while choosing any antibiotics? - Does the aggressive promotional campaign by Pharmacy Company influence your prescriptions?

B. View on Antibacterial Resistance

7. Could you please share your thoughts on antibacterial resistance?
   - Have you come across such a case?
   - In your opinion what are the factors responsible for antibiotic resistance?
   - Irregular dose or course
   - Factors prevent antibiotic resistance.
8. What is your opinion on antibiotic combinations available in the market?
   - Do you use them? If yes in which conditions?
   - What are the common combinations available here?
   - Do they help in preventing antibiotic resistance?
9. Many medicine company are enter the pharmacy industry, but the quality control is not of absolute surety. Do you feel antibiotics from not so reputed company are responsible for poor antibiotic response?
10. What is your opinion regarding nonhuman use of antibiotics?
    - Is it create any resistance problem in humans?
    - If so how?
    - In poultry as growth promoter
    - In dairy farm

C. Environmental issue of Antibiotics

11. Is environmental condition affecting your prescription?
    - Local climate (forest, costal area)
    - Seasons (weather, temperature)
    - Pollution
    - Population density
12. What is your opinion regarding antibacterial resistance with respective to environment?
13. Do the medical wastes contain any antibiotics? Is it creating any problem to environment as well as humans?

I have agreed to the interview. I have read all the discussion questions. My name may or may not have confidential.

Signature of Interviewer Signature of Interviewee

SET –B
Veterinarians

Name: Place:
Profession: Interview Date:
Office Address: Starting Time:
Ending Time:

Age:
Sex:
Experience:

A. Knowledge and Practice in Prescribing Antibiotics

Introductory questions	**Probing Area questions**
1. What are the common veterinary diseases in this locality?	- Do they need antibiotics?
2. What are the common antibiotics do you prescribe?	- Name of the antibiotic - Route, Dose, Course
3 .How do you choose antibiotics while prescribe?	- Therapeutic, Prophylactic - Growth promoters (Name, dose, course)
4. What are the common antibiotics used in poultry?	
5. What are the common antibiotics used in dairy farm?	

B. View on Antibacterial Resistance

6. Could you please share your thoughts on antibacterial resistance?
   - Have you come across such a case?
   - In your opinion what are the factors responsible for antibiotic resistance?
   - Factors prevent antibiotic resistance
7. Do you think nonhuman use of antibiotics create any resistance problem in human? If so how?
8. When more antibiotics are used in dairy farm is there any change in quality of the milk?
9. What is your view regarding growth promoters in animals and antibiotics resistance?

C. Environmental issue of Antibiotics

10. Is environmental condition affecting your prescription?
    - Local climate (forest, costal area)
    - Seasons (weather, temperature)
11. What is your opinion regarding antibacterial resistance with respective to environment?
12. Do the medical wastes contain any antibiotics? Is it creating any problem to environment as well as humans?

I have agreed to the interview. I have read all the discussion questions. My name may or may not have confidential.

Signature of Interviewer Signature of Interviewee

SET –C
Drug sellers

Place:
Interview Date:
Starting Time:
Ending Time:

Name:
Profession:
Office Address:

Age:
Sex:
Experience:

A. Knowledge and Practice in Selling Antibiotics

Introductory questions	**Probing Area questions**
1. What are the antibiotics available in your shop?	- Which are most common? - Which antibiotics are sold maximum in your counter?
2. What you do when you get a patient directly come to you for his illness?	- Do you supply antibiotics to the Patients without prescription? - Are they complete their full course?
3. There are lot of Pharmacy Company and various brands with same composition in the market. How you choose your medicine from stockist?	

B. View on Antibacterial Resistance

4. Do you have any idea regarding nonhuman use of antibiotics? (Cattle, poultry, horticulture, agriculture or other)
5. What is your view regarding antibiotic use and antibacterial resistance?

C. Environmental issue of Antibiotics

6. Is environmental condition affecting your selling?
   - Seasons (weather, temperature)
7. How do you dispose the expired medicines?

I have agreed to the interview. I have read all the discussion questions. My name may or may not have confidential.

Signature of Interviewer Signature of Interviewee