

The Ghanaian-Dutch Collaboration for Health Research and Development

RESISTANCE TO ANTIMICROBIAL DRUGS IN GHANA

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SUMMARY

There is inadequate information in Ghana on the susceptibility of microorganisms to antimicrobial agents used for treatment of patients. The study was, therefore, carried out to establish the antibiogram of bacterial agents causing infections in the country. The study was carried out in nine of the ten regions in Ghana, and various hospitals including two teaching hospitals, seven regional hospitals, and two district hospitals.

The study was a quantitative type. A total of 5099 bacterial isolates from various clinical specimens of patients, and data related to the patients were collected from the hospitals over a period of one year from December, 2002 to December, 2003. The isolates were identified by culture and biochemical reactions, and the Kirby Bauer method was used to test their susceptibility to various antimicrobial agents. In addition, the minimum inhibitory concentration (MIC) of some of the multiple resistant isolates of epidemiological significance was also determined using the E-test.

Main findings and conclusions

A wide range of bacterial isolates were identified in both teaching and regional hospitals, most of which were enterobacteria. Fastidious organisms were more associated with the infections in the teaching hospitals. High percentage of resistance was observed for tetracycline (82 per cent), cotrimoxazole (73 per cent), ampicillin (76 per cent) and chloramphenicol (75 per cent). Several isolates especially enterobacteria had multiple drug resistance to a combination of ampicillin, tetracycline, chloramphenicol and cotrimoxazole. On the other hand, a lower percentage of resistance was observed for ceftriazone (6.3 per cent), ciprofloxacin (11 per cent) and amikacin (9.9 per cent). Generally, the prevalence of multiple drug resistance (resistance to three or more drugs) was widespread among the various isolates and some multiple resistant strains of *Staphylococcus aureus*, *Salmonella typhi*, and non typhoidal *Salmonella* had high MIC to cefuroxime (>256), gentamicin (>256), and ciprofloxacin (>32).

Recommendations

1. Adequate laboratory inputs and trained technologists/technicians must be provided for the regional hospitals so that they can do culture identification and sensitivity tests of both fastidious and non-fastidious organisms by internationally approved methods.
2. Technicians/technical assistants in the regional hospitals must be trained on site to be able to optimally use the available facilities for investigation of infection.
3. Fastidious organisms must be collected from all regions and tested for their susceptibility to antimicrobial agents.
4. Investigation of infection at all levels in the health service must be encouraged to find the current causative agents for specific disease complexes e.g. lower tract respiratory infections, genital discharge/genital ulcers etc.
5. General practitioners must be encouraged or if necessary assisted to investigate causes of infection, to provide information on causes of community infections.
6. Equipment and supplies needed for culture and sensitivity of especially anaerobic bacteria must be provided in the teaching and regional hospitals in order to provide a complete picture of the causative agents of infection.
7. Re-evaluation of the indications for the use of ampicillin, tetracycline, chloramphenicol and cotrimoxazole in the treatment of infection in Ghana is needed in view of the high levels of resistance observed.
8. The use of fluoroquinolones and 3rd generation cephalosporins in Ghana must be controlled by restricted prescription so as to extend their useful 'life span'.
9. Since typhoid fever is a major problem in Ghana, a large number of isolates of *S. typhi* needs to be collected for determination of MIC in order to have as much information as possible on *S. typhi* strains in Ghana.
10. Laws (already available in Ghana) on the sale

of antimicrobial agents in the country must be enforced.

11. The public must be educated on the use and misuse of antimicrobial agents, through the print and electronic media.
12. The use of standard methods of sensitivity testing must be enforced in all laboratories to facilitate the generation of data which could be used for laboratory based surveillance of susceptibility.
13. With the support of WHO-AFRO, a comprehensive national plan for laboratory based sentinel survey of susceptibility and drug use/ consumption data from various sources must be set up in Ghana.
14. A national coordinating committee to monitor progress of the surveillance programmes must be established.

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LIST OF ABBREVIATIONS

KATH	Komfo Anokye Teaching Hospital
KBTH	Korle Bu Teaching Hospital
SMS	School of Medical Sciences
KNUST	Kwame Nkrumah University of Science and Technology
UGMS	University of Ghana Medical School
WHO	World Health Organisation
µg/ml	micro grams per milliliter
Fig	figure
Staph	<i>Staphylococcus</i>
Strept	<i>Streptococcus</i>
E. coli	<i>Escherichia coli</i>
Sal.	<i>Salmonella</i>
N.	<i>Neisseria</i>
Spp.	Species
E-strip	E test strip for MIC test

Chapter One

INTRODUCTION

Bacterial infections constitute an important cause of morbidity and mortality among human beings all over the world. For decades, antimicrobial drugs have proven useful for treatment of bacterial infections. Although some bacteria are inherently resistant to even newly developed antimicrobial agents, the emergence of acquired resistance to antimicrobial drugs had been observed in almost all pathogenic bacteria^{1,2}. Antimicrobial resistance has become an important public health problem associated with serious consequences for the treatment of infection. This ultimately affects both economic and social development. The problem has been attributed to the misuse of antimicrobial drugs which provide selective pressure favouring the emergence of resistant strains. To contain the problem of antimicrobial resistance, the World Health Organisation has provided some interventions. These include creating a national task force, developing indicators to monitor and evaluate the impact of antimicrobial resistance, and designing reference microbiological facilities that would coordinate effective surveillance of antimicrobial resistance among common pathogens. While these interventions seem to have been well implemented in the developed world, lack of resources constrains implementation in many developing countries where treatment options also tend to be relatively limited. Thus, though a global problem, antimicrobial resistance tends to be more significant in developing countries than in the developed world.

Several studies in African countries had reported the presence of resistant strains of bacteria, these include reports from Ethiopia³, Nigeria^{4,5}, Benin⁶, Uganda⁷, Kenya⁸, Zimbabwe⁹, Senegal¹⁰, and South Africa¹¹, all showing high levels of resistance to antimicrobial agents. Most of these reports show bacterial resistance to commonly utilised and relatively cheap drugs like ampicillin, tetracycline and cotrimoxazole which had been the main stay of antimicrobial treatment in Africa for decades.

In Ghana, antimicrobial therapy constitutes a major form of treatment and it is mainly empirical

due to a relative lack of appropriate laboratory facilities for culture and sensitivity testing of bacteria in several health facilities. Even, where laboratory facilities are available, culture and sensitivity tests may not be requested due to the fact that it is an extra cost to be paid by the patient. Studies on drug resistance had been reported mainly from the two teaching hospitals in Accra - KBTH¹²⁻¹⁶ and Kumasi - KATH¹⁷⁻¹⁸ and hardly any from the regional and district hospitals. Thus there is inadequate information on the susceptibility of microorganisms to antimicrobial agents used for treatment in several areas in Ghana. Syndromic treatment had been established for infections like sexually transmitted diseases and respiratory tract infections. Without surveillance records of antimicrobial susceptibility, empirical treatment could be ineffective and expensive. Unfortunately, there is hardly any system of monitoring and controlling antimicrobial use in the country. There is, therefore, the need to develop a surveillance system to address these problems which could go a long way to reduce morbidity and mortality associated with bacterial infections in the country.

OBJECTIVES

- The objectives of the study are to
- (i) identify the agents of bacterial infections in Ghana.
 - (ii) establish the antibiogram of these bacteria and determine the minimum inhibitory concentration of multiple drug resistant bacteria of epidemiological importance.
 - (iii) Set up a surveillance programme for bacterial infections and antimicrobial resistance.

Research question

What are the prevailing bacterial agents involved in infections in Ghana, and the current incidence of antibiotic resistance of these agents?

Chapter Two

MATERIALS AND METHODS

Study area and collection of bacteria isolates

The study was carried out in nine of the ten regions in Ghana. Hospitals with facilities for culture and sensitivity testing in the regions were selected for the study. The hospitals selected included two teaching hospitals, seven regional hospitals and two district hospitals. Arrangements were made with the selected hospital for collection and storage of bacteria isolated from clinical specimen of patients. Fastidious bacteria were stored in trypticase soy broth with glycerol at 4°C, while non-fastidious bacteria were stored on nutrient agar slopes at 4°C. Relevant information on patients from whom isolates were obtained was also collected. This included age, sex, diagnosis and the type of specimen. The isolates and data collected were transported at regular intervals to the Korle-Bu Teaching Hospital (KBTH) in Accra or the Komfo Anokye Teaching Hospital (KATH) in Kumasi for analysis. Isolates from Sunyani Regional Hospital were sent to KATH while isolates from the other sites were sent to KBTH. Isolates from KATH were tested by standard procedures as those in Accra. Isolates received from the regions, were retested at KBTH. Bacteria isolates were collected from December 2002 to December 2003 from the various hospitals as shown in Appendix 1.

Laboratory analysis

Laboratory tests on isolates involved biochemical identification and sensitivity testing. Firstly, the isolates were identified by culture and biochemical tests. Following this, the Kirby Bauer method of sensitivity testing was employed to determine the antibiogram of the isolates using the following 16 antimicrobial drugs with their disk content in

microgram (ug):- ampicillin (10), tetracycline (30), cotrimoxazole (25), chloramphenicol (30), gentamicin (30), amikacin (30), cefuroxime (30), cefotaxime (30), ceftriazone (30), penicillin (10), erythromycin (15), cloxacillin (5), ciprofloxacin (5), norfloxacin (10), nalidixic acid (30) and nitrofurantoin (300), all commonly used in Ghana. The E-test was used to determine the minimum inhibitory concentration (MIC) of epidemiologically significant isolates identified as multiple drug resistant. The antimicrobial agent used for the E-test was based on the susceptibility pattern of the isolate. Such bacteria included *Staphylococcus aureus*, *Salmonella typhi*, non-typhoidal *Salmonella*, *Shigella* spp and *Vibrio cholerae*.

For quality assurance, the methodologies employed were standard ones, and isolates from the regions were retested for confirmation of their identification and antibiotic susceptibility.

The biochemical identification and sensitivity report collected from the regions were compared with the results obtained from KBTH.

Data analysis

Laboratory results and data collected on patients were entered into MICROSOFT-EXCEL and analysed in STATA 7.0 to address the objectives of the study. This involved descriptive analysis including frequencies and prevalence rates of resistance of the different bacteria. The bacterial agents were categorised as sensitive or resistant. Frequencies and prevalence rates were calculated for resistant and multiple resistant bacteria agents including their antibiogram. In addition, the mean inhibitory concentrations (MIC) of multiple resistant bacteria were also determined.

Chapter Three

FINDINGS

A total of 5099 isolates were collected from the various hospitals. The bacteria were mainly Gram negative organisms with *Escherichia coli* being the commonest, followed by *Staphylococcus aureus*, *Klebsiella* species and *Pseudomonas aeruginosa*. These four organisms made up 56 per cent of the organisms studied as listed in Table 1.

Table 1
List of bacteria isolates

Bacterial agent	Overall	
	N	%
<i>Escherichia coli</i>	1105	21.7
<i>Staphylococcus aureus</i>	788	15.5
<i>Klebsiella</i> spp.	536	10.5
<i>Pseudomonas aeruginosa</i>	441	8.7
<i>Proteus</i> spp.	397	7.8
<i>Enterobacter</i> spp.	275	5.4
Non tyhoidal <i>Salmonella</i>	247	4.8
Other <i>Streptococcus</i> spp.	127	2.5
<i>Citrobacter</i> spp.	120	2.4
<i>Salmonella typhi</i>	109	2.1
<i>Acinetobacter</i> spp.	88	1.7
<i>Streptococcus pneumoniae</i>	51	1.0
<i>Neisseria gonorrhoeae</i>	17	0.3
<i>Neisseria meningitidis</i>	11	0.02
<i>Haemophilus influenzae</i>	4	0.08
<i>Shigella</i> spp.	4	0.08
<i>Vibrio cholerae</i>	1	0.02
Others	778	15.4
Total	5099	100

n represents number of bacterial isolates

% represents corresponding percentage of bacteria isolates

Identify the agents of bacterial infections

Organisms received from the different regions are shown in Fig. 1, 50 per cent were from Ashanti, 38.8 per cent from Greater Accra and all the other seven regions contributed 11.2 per cent of isolates. The isolates were mainly from cultures of blood (1081), urine (1001), wound swabs (889), sputum (317) and high vaginal swab (270), these specimens accounted for approximately 65 per cent of all the specimens from which isolates were studied. Few isolates were received from aspiration of various anatomical sites, urethral swabs, cerebrospinal fluid and stool, as shown in Table 2.

Blood cultures yielded these organisms: *Staph. aureus* (53 per cent), non-typhoidal *salmonella* (19 per cent), *Klebsiella* (11.7 per cent), and *Salmonella typhi* (9.3 per cent).

Urine cultures yielded mainly *E. coli* (66 per cent), *Klebsiella* (12.7 per cent), *Staph. aureus* (6 per cent) and *Pseudomonas* (4 per cent), these accounted for 89 per cent of the urinary isolates.

The wound swabs yielded *Pseudomonas* (23.7 per cent), *Proteus* (21.3 per cent), *Staph aureus* (15.5 per cent), *E. coli* (14.4 per cent) and *Klebsiella* (8.5 per cent), these accounted for 83 per cent of the isolates from wounds.

Sputum cultures grew mainly *Klebsiella* (28.4 per cent), *Enterobacter* (18 per cent), *Pseudomonas* (15.8 per cent), *Citrobacter* (6 per cent), and *E. coli* (11 per cent), these accounted for 79 per cent of the organisms from sputum.

Cerebrospinal fluid isolates were mainly *Strept. pneumoniae* (55 per cent) and *N. meningitidis* (17 per cent). Stool isolates were non-typhoidal *salmonella* (63 per cent) and *Sal. typhi* and *Shigella* spp. 12.5 per cent each, making a total of 86 per cent of stool isolates.

Establish the antibiogram of these bacteria and determine the MIC of multiple drug resistant bacteria of epidemiological importance

Figure 2 shows the overall prevalence of resistance to the antimicrobial agents. There was very high per-

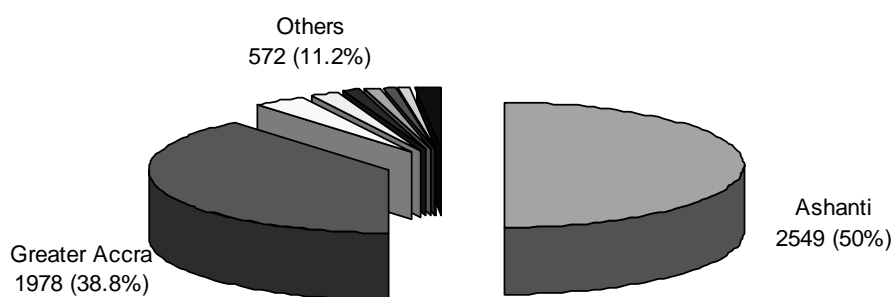


Fig. 1: Numbers of bacterial isolates collected from various regions

Table 2
Numbers of bacteria isolates from various clinical sites

Bacterial agent	N	ws	Blood	Urine	Sputum	Hvs	Aspirate	Csf	Stool	Others
<i>Escherichia coli</i>	1105	128	85	662	35	116	1	3	2	(73)
<i>Staphylococcus aureus</i>	788	138	381	60	16	32	24	2	0	(135)
<i>Klebsiella spp.</i>	536	76	126	127	90	5	2	2	0	(108)
<i>Pseudomonas aeruginosa</i>	441	211	28	40	50	6	2	2	0	(102)
<i>Proteus spp.</i>	397	189	18	42	19	19	3	0	0	(107)
Non typhoidal <i>Salmonella</i>	247	5	209	11	0	0	3	0	15	(4)
<i>Enterobacter spp.</i>	275	62	78	7	58	23	2	3	0	(42)
<i>Salmonella typhi</i>	109	0	101	2	0	0	0	1	3	(2)
<i>Streptococcus spp</i>	127	14	6	21	12	49	1	1	0	(23)
<i>Citrobacter spp.</i>	120	35	10	17	20	18	2	0	0	(18)
<i>Acinetobacter spp.</i>	88	31	30	4	13	1	0	1	0	(8)
<i>Streptococcus pneumoniae</i>	51	0	8	0	4	0	1	35	0	(3)
<i>Neisseria meningitidis</i>	11	0	0	0	0	0	0	11	0	(0)
<i>Neisseria gonorrhoeae</i>	17	0	0	8*	0	1	0	0	0	(8)
<i>Shigella spp.</i>	4	0	1	0	0	0	0	0	3	(0)
<i>Haemophilus influenzae</i>	4	0	0	0	0	0	0	3	0	(1)
<i>Vibrio cholerae</i>	1	0	0	0	0	0	0	0	1	(0)
Total	4321	889	1081	1001	317	270	41	64	24	(634)

N = total isolates; ws = wound swab; hvs = high vaginal swab; csf = cerebrospinal fluid

* isolated from urethral specimen

() bacteria isolated from specimens other than those listed are in bracket

Fig. 2: Prevalence of resistance among antimicrobial drugs

centage resistance to cotrimoxazole (73 per cent), chloramphenicol (75 per cent), ampicillin (76 per cent), and tetracycline (82 per cent), the level of

hospitals. Resistance to gentamicin, cefuroxime and cefotaxime was about 20 per cent., while that of amikacin, ceftriaxone and ciprofloxacin was less than

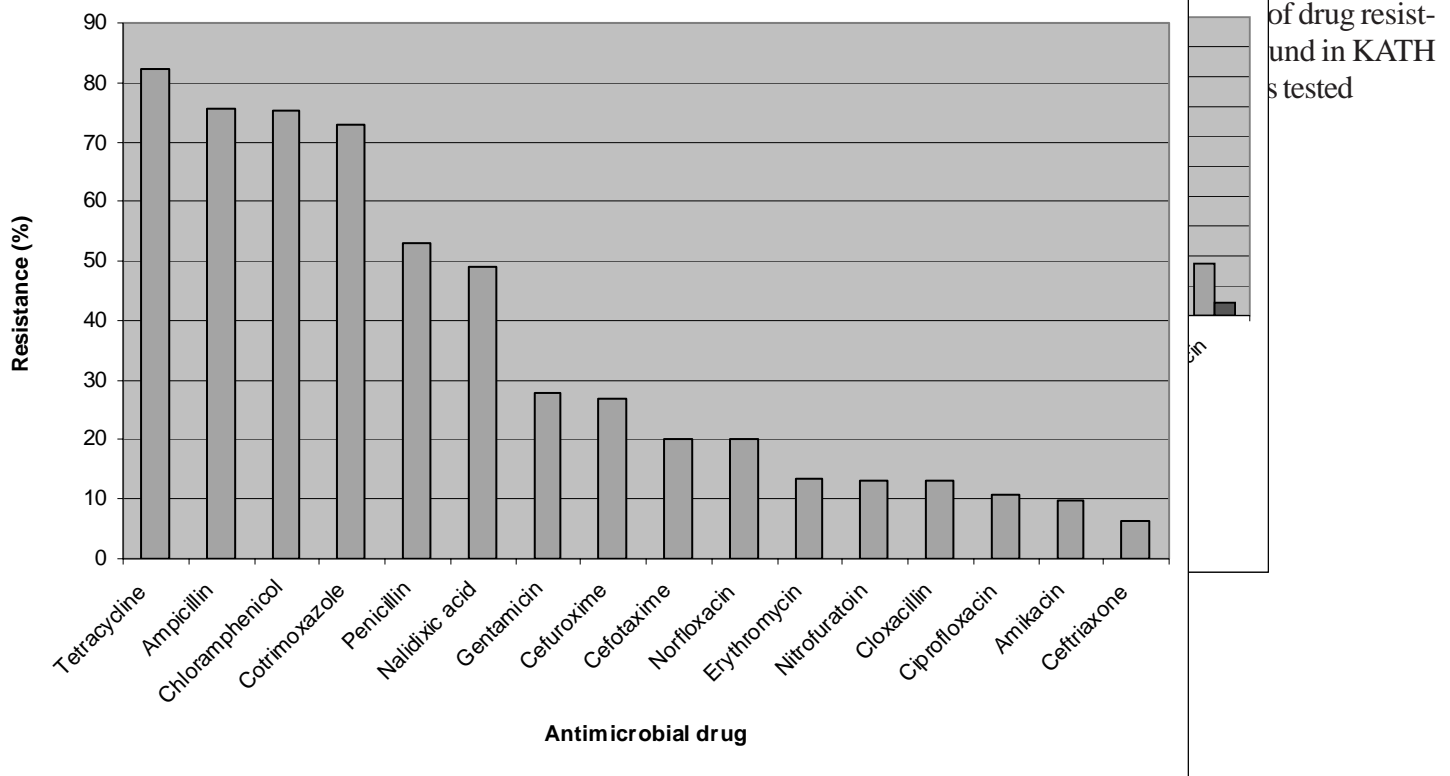


Fig. 3: Prevalence of resistance among antimicrobial drugs in teaching and regional hospitals

Fig. 4: Prevalence of resistance among antimicrobial drugs in the teaching hospitals

Table 3 shows the prevalence of multiple drug resistant (mdr) strains of different types of bacteria. For *E. coli* (70 per cent), were mdr, *Enterobacter*

species (60 per cent), *S. typhi* (62 per cent), *Citrobacter* (65 per cent) and *Staph. aureus* (42 per cent). The prevalence of multiple drug resist-

Table 3
Prevalence of multiple drug resistance among bacterial agents

Bacterial agent	Total isolates	No. of mdr isolates	%mdr isolates
<i>Pseudomonas aeruginosa</i>	441	100	22.7
Other <i>Streptococcus</i> spp.	127	100	78.7
<i>Acinetobacter</i> spp.	88	57	64.8
<i>Citrobacter</i> spp.	120	78	65.0
<i>Streptococcus pneumoniae</i>	51	4	7.8
<i>Escherichia coli</i>	1105	768	69.5
<i>Enterobacter</i> spp.	275	166	60.4
<i>Salmonella typhi</i>	109	68	62.4
Non tyhoidal <i>Salmonella</i>	247	149	60.3
<i>Klebsiella</i> spp.	536	309	57.6
<i>Proteus</i> spp.	397	222	55.9
<i>Nesisseria gonorrhoea</i>	17	2	11.8
<i>Staphylococcus aureus</i>	788	333	42.3

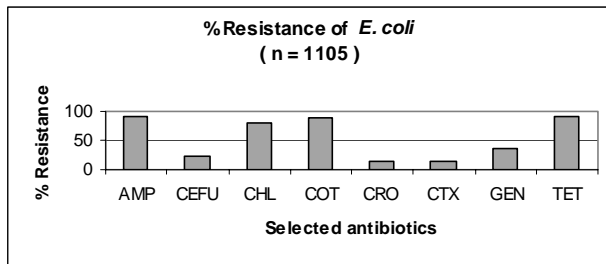
Mdr = multiple drug resistant

ance in specific microorganisms is depicted in Fig 5a to 5h. *Strep pneumoniae* had the lowest percentage of multiple drug resistance. Fig 5h shows that 50 per cent of *Pseudomonas* was resistant to cefotaxime.

Mean inhibitory concentrations (MIC) of selected multidrug resistant microorganisms of epidemiological significance is shown in Table 4. Eighteen isolates of *Staph. aureus* were tested against cefuroxime, the MIC of 10 isolates ranged from 0.25–.0 ug/ml, but 8 isolates had MIC >256 ug/ml. For the same group of isolates, gentamicin MIC range was 0.19–24 ug/ml and 3 isolates had MIC >256 ug/ml.

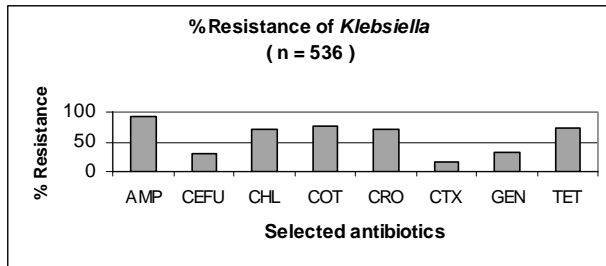
Of the *S. typhi* tested 2/10 also had MIC of >256 ug/ml. Appendix 2a, 2b and 2c show the MICs of the isolates tested.

5a

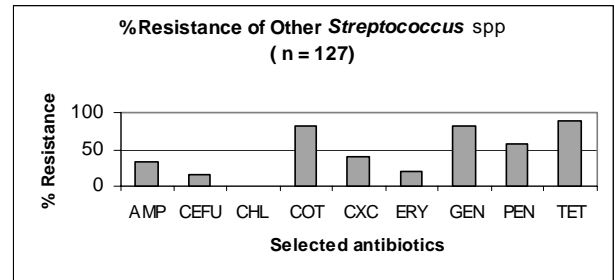


5b

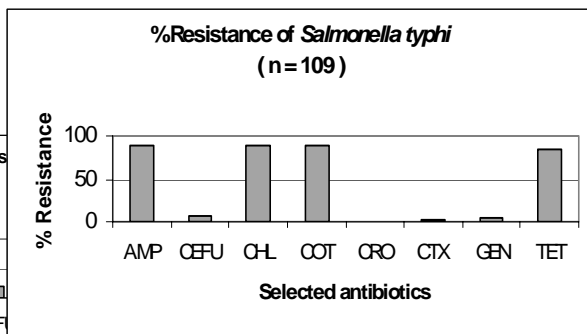
5c



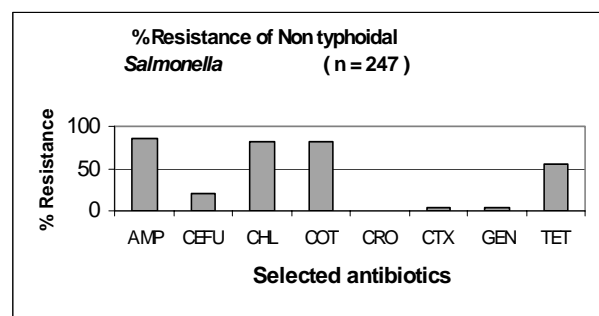
5d



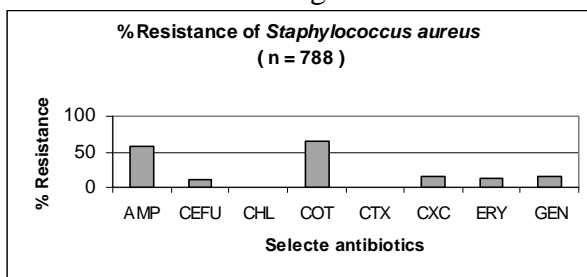
5e



5f



5g



5h

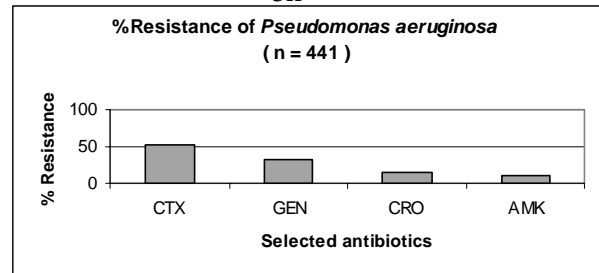


Fig. 5: Percentage resistance of bacterial agents to antimicrobial drugs

AMP- Ampicillin
 CEFU- Cefuroxime
 CHL- Chloramphenicol
 COT- Cotrimoxazole
 CRO- Ceftriaxone
 CTX- Cefotaxime

GEN- Gentamicin
 TET- Tetracycline
 CXC- Cloxacillin
 ERY- Erythromycin
 PEN- Penicillin

Table 4
Minimum inhibitory concentration (MIC) of bacterial isolates

Bacterial agent	N	Antimicrobial drug	RANGE OF MIC (ug/ml)
<i>Staphylococcus aureus</i>	*18	Cefuroxime	0.25-4.0 (* 8 isolates > 256)
	18	Gentamicin	0.19-24.0 (3 isolates >256)
<i>Salmonella typhi</i>	*10	Cefuroxime	1.5-6.0 (* 2 isolates > 256)
	10	Ciprofloxacin	0.004-0.094
	10	Gentamicin	0.19-1.5
Non typhoidal <i>Salmonella</i>	*14	Cefuroxime	3.0-48.0 (* 5 isolates >256)
	14	Ciprofloxacin	0.008-0.38 (1 isolate >32)
	14	Gentamicin	0.25-4.0
<i>Vibrio cholerae</i>	1	Ciprofloxacin	0.094
	1	Cefuroxime	12.000
	1	Ampicillin	64.000
<i>Shigella</i> spp	1	Ciprofloxacin	0.064

Set up a surveillance programme for bacterial infections and antimicrobial resistance.

On retesting of isolates from the regions, the biochemical identification of the organisms was the same as those obtained in KBTH but there were some discrepancies in the sensitivity results. Out of a total

of 387 isolates from the non-teaching hospitals, 150 (39 per cent) had similar results, but the others showed discrepancies in the sensitivity results ranging from 53 per cent in the Bolga regional hospital to 75 per cent in the Tetteh Quarshie Memorial hospital. The level of discrepancies seen in the different regional hospitals is shown in Appendix 3.

Chapter Four

DISCUSSION AND RECOMMENDATIONS

Bacteria causing infections from various specimens including wounds, blood, urine, and high vaginal swabs in Ghana were identified as including *E. coli*, *Staph aureus*, *Klebsiella*, *Pseudomonas* and *Salmonella* species. The number of isolates from seven regions was only 11.2 per cent of the total while organisms from Ashanti and Accra were 50 per cent and 38.8 per cent respectively. This is likely to create some biases in the analysis. While the low collection of bacteria from the regions could be due to relatively fewer patients visiting these facilities and, therefore, fewer cultures, it was also observed that culture and sensitivity testing of bacteria may not have been done on regular basis as a result of lack of inputs like petri dishes and media required for culture. In some instances there was only one person who could handle the specimens competently and, therefore, if that person was not at post, then culture may be suspended for a period. Most of the isolates from the regions were Gram negative rods e.g. enterobacteria and *Pseudomonas*. The fastidious organisms like *Streptococcus pneumoniae*, *Neisseria gonorrhoea* and *Haemophilus species* were collected in the teaching hospitals. This inability to isolate fastidious organisms in some regional hospitals, is due to lack of particular/special media and other requirements for culture and identification or due to lack of technical expertise.

In view of the fact that patients had to pay the cost of their investigations, invariably only a relatively small portion of all cases with an infection had cultures taken to determine the causative agent. In addition, when an infection seems to be serious, it was more likely to be investigated especially if the patient was not responding to treatment. These are sources of limitation for the study because in the ideal situation, one needs to investigate many episodes of a particular infection to determine the types of causative agent(s).

Anaerobic bacteria were not collected from any of the hospitals. Although KBTH and KATH had trained personnel, their inability to culture anaerobes is due to the fact that it is very expensive

to acquire Gaspak etc for generation of anaerobic environment for the culture of anaerobes.

Recommendations

1. Adequate laboratory inputs and trained technologists/technicians must be provided for the regional hospitals so that they can do culture identification and sensitivity tests of both fastidious and non-fastidious organisms by internationally approved methods.
2. Technicians/technical assistants in the regional hospitals must be trained on site to be able to optimally use the available facilities for investigation of infection.
3. Fastidious organisms must be collected from all regions and tested for their susceptibility to antimicrobial agents.
4. Investigation of infection at all levels in the health service must be encouraged to find the current causative agents for specific disease complexes e.g. lower tract respiratory infections, genital discharge/genital ulcers etc.
5. General practitioners must be encouraged or if necessary assisted to investigate causes of infection, to provide information on causes of community infections.
6. Equipment and supplies needed for culture and sensitivity - of especially anaerobic bacteria - must be provided in the teaching and regional hospitals in order to provide a complete picture of the causative agents of infection.

The prevalence of drug resistance among the bacteria was high. Four antimicrobial agents had very high prevalence of resistance, namely tetracycline (82 per cent), ampicillin (76 per cent), chloramphenicol (75 per cent), cotrimoxazole (73 per cent), and for these drugs, the prevalence of resistance is higher in the regions than in the teaching hospitals.

In addition, these are drugs which had been reported as having high percentage resistance for a lot of microorganisms for several years¹⁶. The rate

of resistance had been rising over the years not only for clinical isolates but also for the normal intestinal flora^{16,19} of the healthy population. Comparison of the teaching hospitals show that in almost all the drugs tested, prevalence of resistance is higher in KBTH than in KATH.

Lower prevalence of resistance was found for gentamicin (28 per cent), cefuroxime (27 per cent), cefotaxime and norfloxacin (20 per cent). The lowest prevalence of resistance of between 6 and 10 per cent was found in ciprofloxacin, amikacin and ceftriaxone - these are drugs which had been on the Ghanaian market for a relatively short period of time as compared to drugs like ampicillin and chloramphenicol. In addition, ciprofloxacin, amikacin and ceftriaxone are very expensive drugs and are usually prescribed for serious infections. This might be one of the reasons for the relatively low levels of resistance. It must be noted however that, resistance to the fluoroquinolones -like ciprofloxacin and ofloxacin had been rising^{16,20} and since the mechanism of resistance is by mutations in the DNA gyrase, resistance to one may extend to other fluoroquinolones. It is therefore necessary to try and control the use of these agents so as to maintain their effectiveness for a longer period.

Resistance to antimicrobial agents is a bacteria characteristic carried on genes. The resistant genes present in intestinal flora are transferable to pathogenic bacteria in the intestines. Plasmid-mediated resistance is more easily transferred than chromosomal genes. Olukoya *et al*, in a Nigerian study²¹, detected plasmids with resistance to tetracycline, streptomycin, ampicillin and cotrimoxazole in *Shigella* species. In Ghana, a study by Mills-Robertson *et al*²² of plasmids in *Salmonella*, reported their location on conjugative plasmids. The plasmids could have evolved because of antibiotic misuse. There is antibiotic misuse by the general public due to easy availability of drugs without prescription, or by physicians, through poor prescribing habits.

In this study, we did not differentiate between organisms from community acquired infections and those from hospital infections. A study in Kenya showed that organisms from the community and those from hospital infections had the same patterns of multiple drug resistance.⁸ It may be

necessary in future to compare the susceptibility of community and hospital isolates of bacteria.

In view of the low numbers of some organisms like *Haemophilus*, *Neisseria* and *Vibrio*, it was difficult to comment adequately on their findings. It may, therefore, be necessary to collect some more in the near future and analyse their results. Although very few isolates of *N. gonorrhoea* were received, studies in other African countries show that resistant strains are endemic in Africa²³, isolates from sex workers are multiple drug resistant²⁴, and in one report a bacteria strain was found to be resistant to eight different antimicrobial agents²⁵. All these studies show that local surveillance is necessary to help decision making in relation to syndromic treatment and implementation of control measures.

Although only a few of the epidemiologically significant isolates had their MIC's detected, 8/18 *Staph aureus* tested had cefuroxime MIC >256 ug/ml, and three of the same strains had gentamicin MIC >256 ug/ml. Seven of the 24 (7/24) isolates of the *Salmonella* tested also had cefuroxime MIC >256 ug/ml. These microorganisms are highly resistant, and this gives cause for concern. There is, therefore, the need for a bigger study of MIC's of epidemiologically significant clinical isolates.

Recommendations

7. Re-evaluation of the indications for the use of ampicillin, tetracycline, chloramphenicol and cotrimoxazole in the treatment of infection in Ghana is needed in view of the high levels of resistance observed.
8. The use of fluoroquinolones and 3rd generation cephalosporins in Ghana must be controlled by restricted prescription so as to extend their useful 'life span'.
9. Since typhoid fever is a major problem in Ghana, a large number of isolates of *S. typhi* needs to be collected for determination of MIC in order to have as much information as possible on *S. typhi* strains in Ghana.
10. Laws (already available in Ghana) on the sale of antimicrobial agents in the country must be enforced.
11. The public must be educated on the use and misuse of antimicrobial agents, through the print and electronic media.

Due to the changing nature of antimicrobial susceptibility, and the anecdotal evidence of antimicrobial misuse, it is necessary to have locally generated susceptibility results for surveillance purposes. For this study, isolates were collected and retested to find out if the results were comparable. Visiting the various hospitals for collection of samples was time consuming and expensive. Therefore, it will not be cost effective and easy to use this methodology over a long period of time. It will be easier if all the testing is done using standardised procedures at the site of isolation of the organisms. Results could then be forwarded to a centre for analysis. Unfortunately, the finding of quite a lot of discrepancies in the sensitivity results indicate that, it will be necessary to have the same standardised method of sensitivity testing at all the laboratories in the regional hospitals, before a lab-based surveillance could be done.

Recommendations

12. The use of standard methods of sensitivity testing must be enforced in all laboratories to

facilitate the generation of data which could be used for laboratory based surveillance of susceptibility.

13. With the support of WHO-AFRO, a comprehensive national plan for laboratory based sentinel survey of susceptibility and drug use/ consumption data from various sources must be set up in Ghana.
14. A national coordinating committee to monitor progress of the surveillance programmes must be established.

Dissemination

A dissemination meeting would be held to present the findings of the study. This would involve stakeholders, particularly representatives from the Ghana Health Service such as medical directors and the head of Division of Institutional Care.

Chapter Five

CONCLUSIONS

Most of the bacteria from the regions were of the Enterobacteria group e.g. *E. coli* and *Klebsiella* in addition to *Pseudomonas* and *Staph aureus*. A more varied group of organisms were isolated from the teaching hospitals, where the laboratories were able to grow fastidious microorganisms like *Haemophilus*, *Neisseria* and *Streptococci*. For most of the fastidious organisms, the number of isolates studied was relatively few. None of the bacteria collected were anaerobes.

The Enterobacteria isolates were resistant to four commonly used drugs-ampicillin, cotrimoxazole, tetracycline and chloramphenicol, and 50 per cent to 70 per cent of them were multiple drug resistant (depending on the species). Only *Klebsiella* species had high percentage resistance to ceftriaxone. Fifty per cent of *Streptococcus pneumoniae* and 70 per cent of the other *Streptococcal* species were resistant to gentamicin. For almost all the antimicrobial agents, prevalence of resistance is higher in KBTH than in KATH. The prevalence of resistance in the regions is higher than in the two teaching hospitals.

Some of the *Staph aureus* isolates had MIC to gentamicin and cefuroxime which were >256 ug/

ml. These high MIC's were also detected in some *Salmonella* species.

All the isolates tested had very low MIC to ciprofloxacin with the exception of one isolate of non-typhoidal *Salmonella* with an MIC of > 32 ug/ml.

Our reason for collecting and comparing results on the isolates from the regions was to analyse the reports and find out if they could be used for lab-based surveillance. In view of the high discrepancies in the sensitivity results, it will not be prudent to set up a surveillance programme now, by collecting results from the regions for analysis. Reasons for the discrepancies had to be detected and corrected before a system could be instituted.

Interaction with the regional hospitals showed that, although almost all the laboratories indicated that the Kirby Bauer method was used for sensitivity tests, only Holy Family and Tetteh Quarshie hospitals used controls. In addition, some laboratories use the flooding method (to put isolates on the media). This means that they were not using standardised methods.

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APPENDICES

Appendix 1

Collaborating technologists/technicians in the regional and district hospitals

HOSPITAL	NAME OF TECHNOLOGIST/TECHNICIAN
Central Regional Hospital	Mr. Charles Ampeah
Efia Nkwanta Regional Hospital	Mr. Franklin Aryee
Volta Regional Hospital	Mr. Easabus Deku
Koforidua Regional Hospital	Ms. Francisca Dzata
Holy Family Hospital	Sister Marcelina Gruza
Tetteh Quarshie Memorial Hospital	Mr. Kennedy Sakyi
Tamale Regional Hospital	Mr. Seth Sarpong
Bolgatanga Regional Hospital	Mr. Emmanuel Adongo
Sunyani Regional Hospital	Mr. Richard Bannerman
Komfo Anokye Teaching Hospital	Mr. Ishmael Tetteh

Appendix 2 A

MIC of *Staphylococcus aureus* (n= 18)

MIC ug/ml	CXM	GEN
0.125	0	0
0.19	0	1
0.25	1	2
0.38	1	1
0.5	2	0
0.75	1	5
1	1	0
1.5	2	0
2	1	1
3	0	0
4	1	0
6	0	1
8	0	0
12	0	0
16	0	2
24	0	1
32	0	0
>256	8	4

- E strip range for CXM and GEN are 0.023-256 ug/ml but MIC of isolates was in the range sho

Appendix 4
Number of isolates from the various regions

Appendix 2 B
MIC of *Salmonella typhi* (n=10)

MIC ug/ml	CXM	GEN	MIC ug/ml	CIP
0.125	0	0		
0.19	0	1		
0.25	0	2		
0.38	0	2	0.002	0
0.5	0	0	0.003	0
0.75	0	4	0.004	2
1	0	0	0.006	0
1.5	4	1	0.008	1
2	0	0	0.012	0
3	1	0	0.016	3
4	2	0	0.023	1
6	1	0	0.032	0
8	0	0	0.047	0
12	0	0	0.064	2
16	0	0	0.094	1
>256	2	0	0.125	0

-E strip range for CIP is 0.002-32 ug/ml but MIC of isolates were in the range shown in table

-E strip range for CXM and GEN are 0.023-256 ug/ml but MIC of isolates were in the range shown in table

Appendix 2 C
MIC of Non - typhoidal *Salmonella* (n = 14)

MIC ug/ml	CXM	GEN	MIC ug/ml	CIP
0.125	0	0	0.004	1
0.19	0	0	0.006	0
0.25	0	1	0.008	2
0.38	0	1	0.012	4
0.5	0	3	0.016	3
0.75	0	4	0.023	1
1	0	2	0.032	0
1.5	0	0	0.047	0
2	0	0	0.064	0
3	3	2	0.094	0
4	4	1	0.125	0
6	2	0	0.19	0
8	0	0	0.25	1
12	0	0	0.38	1
>256	5	0	0.5	0
			>32	1

-E strip range for CIP is 0.002-32 ug/ml but MIC of isolates were in the range shown in table

-E strip range for CXM and GEN are 0.023-256 ug/ml but MIC of isolates were in the range shown in table

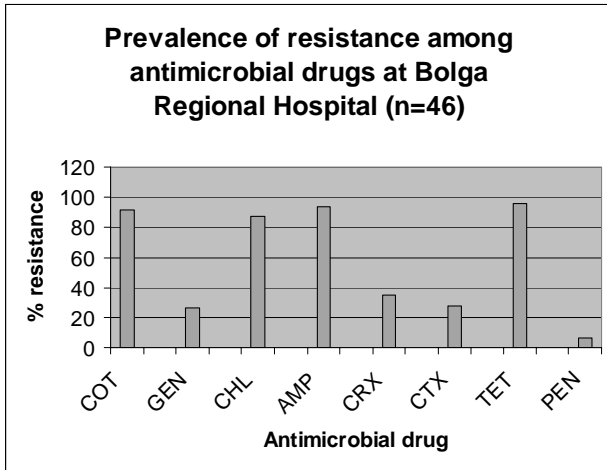
Appendix 3
Discrepancies in sensitivity results from hospitals

Hospital	% discrepancy
Central Regional Hospital	61
Bolga Regional Hospital	53
Efia Nkwanta Hospital	56
Koforidua Regional Hospital	71
Volta Regional Hospital	67
Tamale Regional Hospital	73
Tetteh Quarshie Memorial Hospital	75

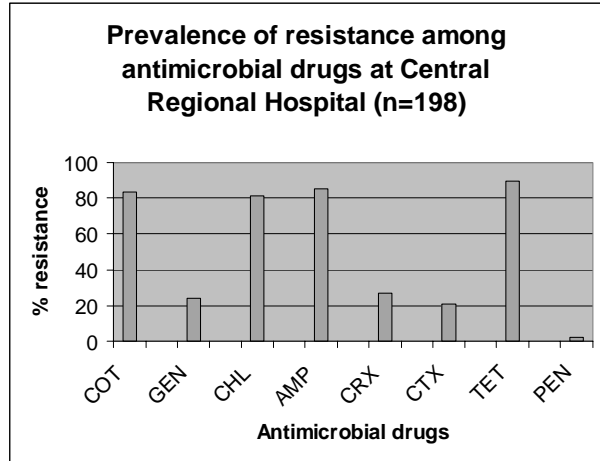
Appendix 4
Number of isolates from various regions

REGION	HOSPITAL	TOTAL ISOLATES
Ashanti	Komfo Anokye Teaching Hospital	2549
Greater Accra	Korle-Bu Teaching Hospital	1978
Central	Central Regional Hospital	191
Volta	Volta Regional Hospital	100
Eastern	Tetteh Quarshie Memorial Hospital	34}
	Koforidua Regional Hospital	29} 86
	Holy Family Hospital	23}
Brong Ahafo	Sunyani Regional Hospital	56
Western	Efia Nkwanta Regional Hospital	50
Upper East	Bolga Regional Hospital	46
Northern	Tamale Regional Hospital	43
TOTAL		5099

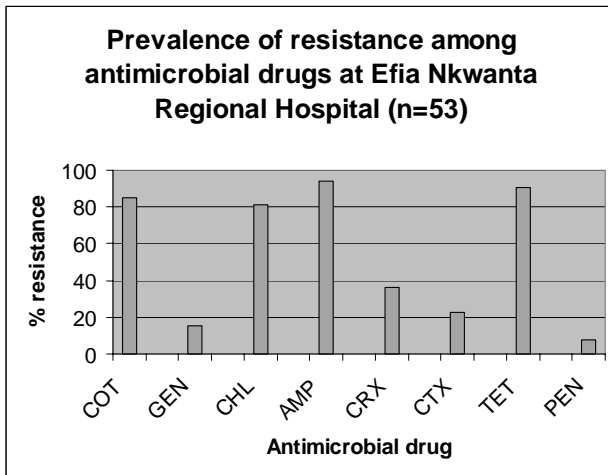
Appendix 5A



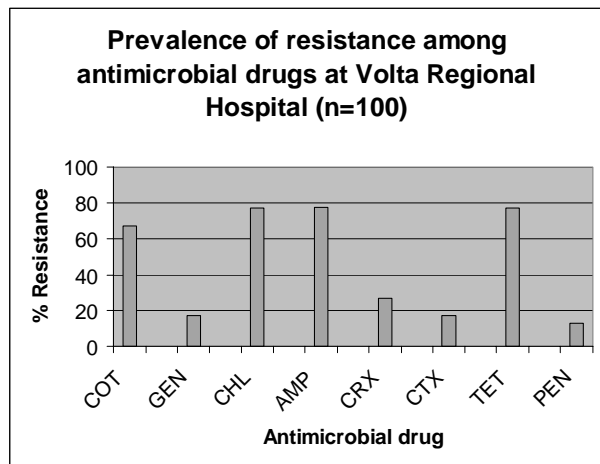
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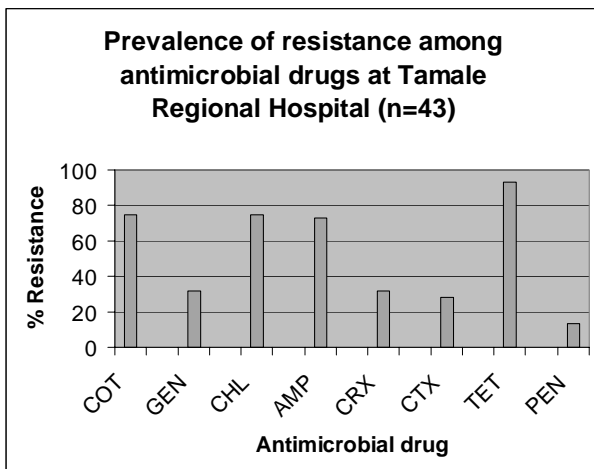
Appendix 5C



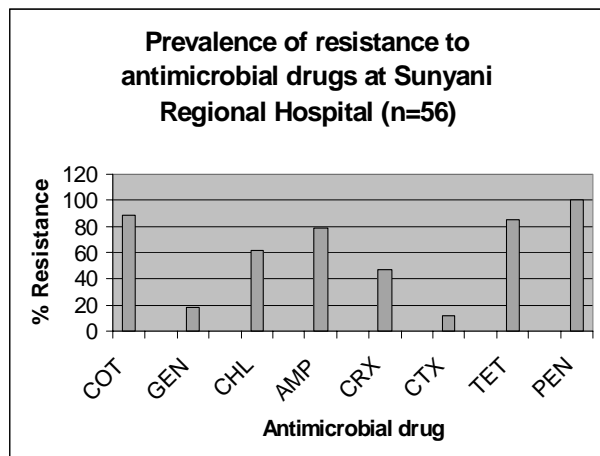
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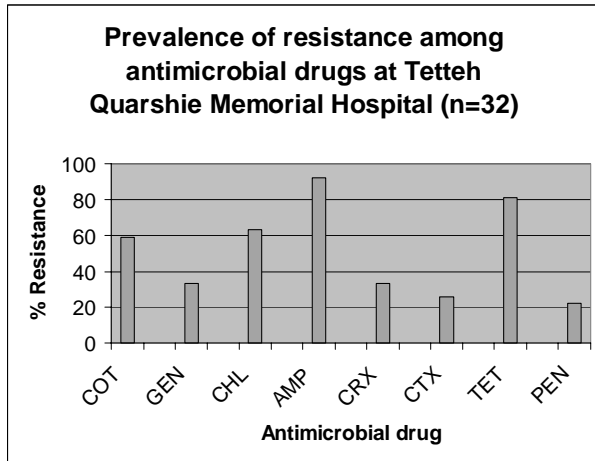
Appendix 5E



Appendix 5F

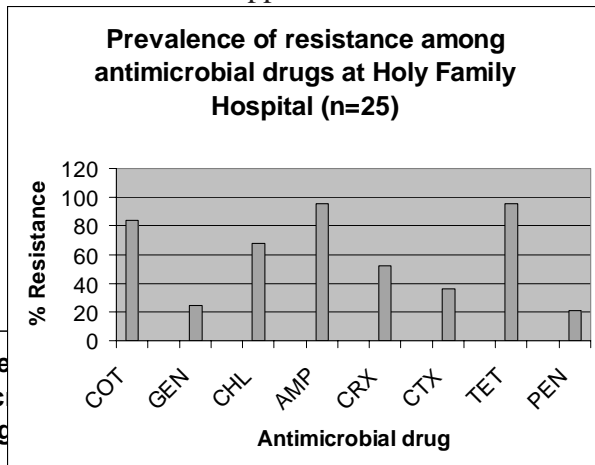


Appendix 5G



Appendix 5H

Appendix 5 I



COT- COTRIMOXAZOLE
 GEN- GENTAMICIN
 CHL-CHLORAMPHENICOL
 AMP- AMPICILLIN
 CRX-CEFUROXIME
 CTX- CEFOTAXIME
 TET- TETRACYCLINE
 PEN-PENICILLIN

