

## Review Article on Antimicrobial Resistance Worldwide

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### Abstract

Antimicrobial is a substance includes antibiotic, anti-fungal, anti-parasite, anti-viruses, that use for the prevention, treatment, of diseases, history of antimicrobial by Egyptians scientist and classification of antimicrobial in a tabular form and some pathological condition related to antimicrobial resistance e.g tuberculosis, urinary tract infection, Typhoid, some key point regarding antimicrobial resistance, and Image related all antimicrobial resistance showed and some mechanism causes of resistance antimicrobial agent, definition of antimicrobial resistance, is an occur when bacteria, fungi, viruses, parasite, change over period and longer response spread, severe illness and death, and factors that influences all anti-microbial resistance and world health organization response regarding antimicrobial resistance, that aims to guide policy makers researchers funder to implementing partners industry, civil society in generating new evidence to inform antimicrobial resistance, and take some review data analysis and graphical showed from region word areas percentage of mortality rate by 2050 AMR, and how to control antimicrobial resistance, by environmental hygiene control and follow medical professional instruction before taken antibiotics, due to avoided risk of resistance of antimicrobial. Also conclusion properly environmental sanitation, using antibiotic by medical professional prescribed, make sure keep diagnosis before start given antibiotics, if reduce the risk factors of resistance antimicrobial agent.

### Introduction

Antimicrobial-including antibiotics, antivirals, anti-fungal and anti-parasitic-all are medicines used to prevent and treat infections in humans, animals and plants infection, Despite proposal initiatives in recent decades, the world has failed to keep with microbes becoming increasingly resistant it's so called Antimicrobial Resistance (AMR) any antibiotic use contributes to have no effect. AMR is thus an unavoidable phenomenon undermine the effectiveness of basic and modern medicine and is effecting people from birth to death [1-10].

Antibacterial Strategic based on metal uptake the rise antibiotic resistance require new strategic to development novel antimicrobial give that bacteria require metal uptake for their survival and proliferation drug that target these uptake path way are a promising approach this section explores how specific metal uptake path way bacteria can used and provides examples of antibiotics that use this strategy.

Also Antimicrobial Resistance (AMR) poses a serious global threat of growing concern to human, animal and environmental health this due to the emergency spread and persistence of multi drug resistance (AMR) bacteria or super bugs MDR bacteria exist across the animal, human an environmental triangle or niche and there is interlinked sharing of these pathogens in this triad.

### History

Antimicrobial was practice use almost 2000 years, ancient Egyptians and ancient Greeks used specific molds and plant extracts for treat infection.

In 19<sup>th</sup> era, microbiologist such as Louis Pasteur and Jules Francois Joubert analyzed antagonism between some bacteria and discussed the merits of controlling this interaction in medicine [11-20].

The Alexander Fleming on September 3, 1928 was isolated staphylococcus separated in to colonies do to the antimicrobial fungus penicillium rubens.

### Classification of antimicrobial

- Antibacterial
- Antivirus

- Antifungal
- Anti-parasite

**Disinfectants:** is an agent used destroyed microorganism in nonliving surfaces. e.g chlorine, calcium, phenol, quatensry ammonium compound etc.

**Antiseptic:** is also applying by living surfaces or during surgery to reduce the infection. e.g Hydrogen peroxide, isopropyl alcohol, chlorhexidine etc.

### What is anti-bacteria?

Is an agent that used for the kill or inhibits the growth of bacteria.

### Spectrum activities

- Narrow spectrum
- Broad spectrum

### Mode of action

- Bacteriacidal
- Bacteriastatic (Table 1)

### Factors influence antibiotic resistance

- Ovar prescription of antibiotic.
- Pateint not finish their treatment.

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**Table 1:** Classification of antibiotics and their uses.

S/n	Classification of Antibiotics	Mode of Action	Mechanism of Action
1	Bete lactam: e.g penicillin, cephalosporin.	Bacteriacidal	Bacteria cell wall inhibit
2	Microlide: e.g Azithromycin, erythromycin	Bacteriastatic	Inhibit Bacteria protein synthesis
3	Aminoglycoside: e.g Amikacin, Streptomycin	Bacteriacidal	Inhibit Bacteria protein synthesis
4	Tetracycline: e.g Doxycycline, minocycline	Bacteriastatic	Inhibit Bacteria protein synthesis
5	Fluroquenolones: e.g Ciprofloxacin, levofloxacin	Bacteriacidal	Target of Bacteria DNA
6	Sulfanamide: e.g Sulfadiazine, sulfadoxine	Bacteriastatic	Inhibit folic Acid Synthesis

**Table 2:** Classification of Antivirus.

S/N	Classification of Antivirus	Enzymes/Mechanism	Targets/Strategies
1	Anti-herpes virus: e.g Acyclovir, vidarabine	polymerase	Viral enzymes
2	Anti-Influenza virus: e.g zanamivir, Amantadine	Neuraminidase	Virus enzymes
3	Anti-hepatitis virus: nonselective drugs e.g adefovir dipivoxil, Ribavir	Capping enzymes, immune response	Cellular target
4	Drug for papilloma: virus e.g imiquimod	Banding to viral glycoprotein	Immuno precipitation

**Table 3:** Classification of Antifungal.

S/N	Classification Antifungal	Mode of Acton	Mechanism of Action
1	Antibiotics e.g Amphotericin B, Griseofulvin	Banding to ergosterol fungicidal	Disruption of spindle and cytoplasmic microtubule fuction.
2	Antimetabolites e.g flucytosine (5-FC)	Inhibit of RNA/DNA protein synthesis	Inhibit fungal protein synthesis by replacing uracil with fluro uracil in fungal RNA.
3	Azoles e.g Imidazole: clotrimazole, miconazole & Triazole: fluconazole, voriconazole	Inhibit of lanosterol 14 alpha-demethylase fungistatic	Inhibit of cytochrome P450.
4	Allylamine: terbinafine	Inhibiting ergosterol synthesis. fungicidal	Inhibit ergo sterol synthesis by inhibiting the enzymes squalene exp oxidase
5	Other topical agent e.g Benzoic Acid, Undercyleneic acid		Miscellaneous, varied

- Over using antibiotic in livestock and fish farming.
- Lack of sanitation and poor hygiene.
- What is Poor infection control in clinical and hospital.

**Antivirus**

Is a substance that can be used for the treating of viruses. e.g. Acyclovir, cidofovir, foscarnet, penciclovir, ganciclovir, brivudin etc (Table 2).

**What is Anti-fungal?**

Is a substance that against fungal infection, like skin. Triazole Anti-fungal: fluconazole, itraconazole, terconazole, Voriconazole etc. e.g. like-Imidazole anti-fungal: ketaconazole miconozolesulconazole, bifonazole, lanaconazole etc (Table 3).

**What is Anti parasite?**

Is a group of substance they can be used for the treatment of diseases coursed by parasite, including protozoa, helminthic. Anti-Helminthic: Albendazole, mebendazole, metronidazole, tinidazole,etc. Anti-Protozoa: quinine, pyramethamine, artemisinin, primaquine etc. can't cost on national and global economies (Table 4).

**Pathological condition related to antibiotics**

- ✧ Typhoid
- ✧ Tuberculosis (TB)
- ✧ Urinary Tract Infection (UTI)

**Typhoid**

Typhoid is an infection that spread through contaminated food and water, cousin by salmonella typhi that change the physiological

function of the body.

**Symptoms:** High fever, headache, abdominal pain, weakness, vomiting, loose of stools.

**Treatment:** Ciprofloxacin, amoxicillin, ceftriaxone, chlorophenicol, cotrimaxazole. These are resistance for the typhoid fever, occur if the bacteria change in repose to use of these medicine.

**TB**

Tuberculosis serious condition course by mycobacterium, primary attack lungs that change the physiological function of the body (Figure 1).

**Symptoms:** Fatigue, fever, loose of appetite, weigh loose, dry cough with blood, shortness of breath, swollen lymph nodes.

**Types of TB:** pulmonary Tb, skeletal Tb, Brain Tb, GIT Tb, miliary Tb,

**Treatment of Tb**

**First line drugs:** Rafampin, isoniazid, ethambutol, pyranamide, streptomycin etc.

**Second line drugs:** levofloxacin, moxifloxacinamikacin, bedaquiline, cycloserine, kanamycin etc.

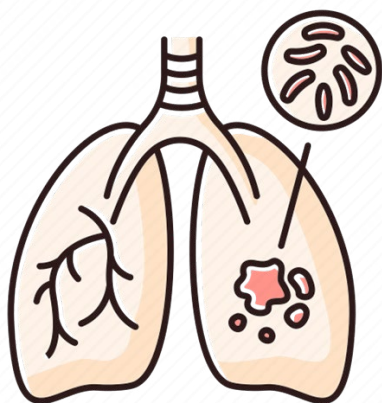
**UTI**

Urinary Tract Infection is a serious infection course by E. coli bacteria usually attack upper and lower urinary track. Upper urinary track: kidney & Lower urinary track: bladder.

**Symptoms:** Pelvic pain, increased urge to urinate, pain with urination and blood in urine, Kidney infection, Back pain, nausea, vomiting, fever.

**Table 4:** Classification of Anti-Parasite.

S/N	Classification of Anti Parasite	Mode of Action	Mechanism of Action
1	Anti-protozoa: e.g metronidazole, Tinidazole,	Destroy protozoa Inhibit the growth and ability to reproduce	Inhibit protozoa folic acid synthesis.
2	Anti-malaria: e.g Quinine, artemisinin,	Inhibit the action heme polymerase.	Interfering with the digestive of haemoglobin in the blood stage of the malaria life cycle,
3	Anti-helmentic: e.g Albendazole, mebendazole,	Inhibit ion of polymerization of beta-botulin into micro tubule followed by inhibition of glucose uptake and transport.	Block micro tubule functions of parasites and mammalian cells.
4	Anti-amobiosis: e.g Chloroquine, tinidazole, metronidazole	Intermediate metabolized compound are formed and bind DNA and inhibit protein synthesis, coursing cell death	Diffuses in to the organism, inhibit protein synthesis by interacting with DNA, and cause a loss of helical DNA structure and strand breakage.



**Figure 1:** Primary attacking lungs.

**Treatment of UTI:** Fluroquenolones, penicilin, cotrimaxazole, tetracycline, cephalosprin, amoxicillin etc.

**Antimicrobial resistance (AMR)**

Is an occur when bacteria, fungi, viruses, parasites, change over period and longer response to the medicines making infections harder to treat and increasing the risk of diseases spread, severe illness and death.

**Keypoint**

- Resistance (AMR) is world health and development threat.
- WHO was declared (AMR) is part of top 10 world public health
- Lack of clean water and proper sanitation
- Without effective antimicrobial the success of modern medicine in treating diseases, including major surgery and cancer chemotherapy, would be at increased risk.

**Why antimicrobial resistance?**

Antimicrobial mostly resistance naturally, genetically occur, and lack of proper used antimicrobial especially antibiotic, over used one class of antibiotic, escaped dose, environmental and sanitation hazard.

**Antibacterial resistance such as antibiotics**

Example anti TB drugs Rafampin. Is an anti TB drug broad spectrum used combine drugs treatment due to avoided resistance e.g. isoniazid, ethambutol, pyrazinamide. Was discovered in 1965, marketed in Italy in 1968 and approved in United State in 1971.

**Mechanism of action:** Rafampin usually inhibit bacterial DNA and

dependent RNA polymerase.

Resistance Rafampin is a broad subject not the mechanism of clinical resistance, nearly always due to genetic change in the  $\beta$  sub unit bacteria RNA Polymerase. In particular mycobacterium Tb interestingly, change in the same codons of the consensus.

**Side effect:** hepatotoxicity, itching, flushing, drowsiness, headache, difficulty concentration etc (Figure 2).

**Note:** Before given Rafampin should being test the liver function and amount of blood in the body.

**Antivirus Resistance**

Is a substance used for the treatment of viruses that courses infection and illness such as: influenza, genital herpes, immunodeficiency virus (HIV), Anti viruses working, a viruses courses infection by entering host cell and making copies of itself (replicating). Antivirus drugs block the viruses ability to replicate.

**Courses resistance antivirous**

The less amount viruses but is always there, if you miss prescribed doses of an antiviral or stop treatment too son the virus may multiplying again As may replicates the virus genetic make-up mutate change. Sometime viruses responding for previously antivirals effective for no known reason called spontaneous resistance (Figure 3).

**Note:** People who take antiviral for long time treatment chronic viral infection like HIV, Genital herpes, hepatitis B or hepatitis C are more risk for virus resistance. Also people have compromised immune system due to autoimmune diseases, organ transplant, cancer treatment chemotherapy more risk of antiviral resistance

**Antifungal resistance**

**Agent:** It help body to get rid certain fungal infection; they treat fungal like skin yeast infection, athletes foot, itch, and ring worm.

**Why Anti-fungal resistance?**

Improper used anti-fungal drugs: e.g. skip doses, stop treatment when you get partial relief, or receive doses low, that fungus may get chance fighting off the medicines effects.

**Natural resistance:** never respond to anti-fungal.

**Spontaneous resistance:** fungus stops responding to once effective drugs for no known reason.

**Transmitted resistance:** if spreads contagious drugs resistance fungal infection to someone else, that person now has not respond anti-fungal, even they have never used the medicine (Figure 4).

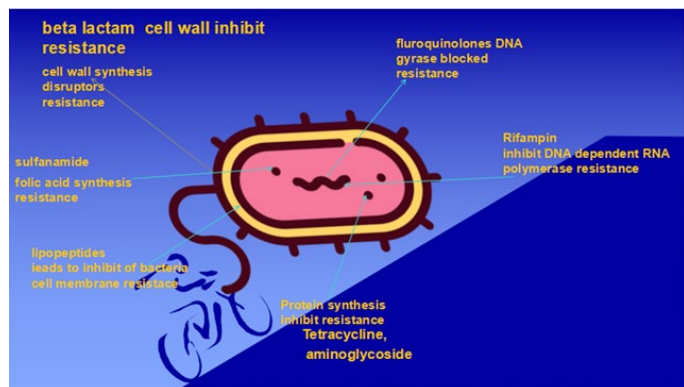


Figure 2: Mechanism of Bacteria Resistance.

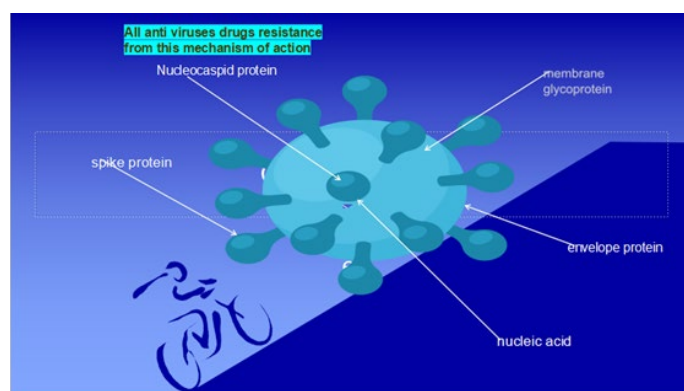


Figure 3: Mechanism of anti-viruses drugs resistance.

### Why anti-fungal resistance is serious global issues?

Because it has greatly limit treatment option, if the anti-fungal does not respond to one of the three classes of anti-fungal drugs, the other option may be less effective, some medication course more severe potentially toxic side effect.

### Who is risk to development anti-fungal resistance?

People leimmuneak system, AIDS, cancer, organ transplant, stem cell (bone marrow) transplant.

### Anti-parasites resistance

Resistance is genetic ability to survive treatment with an anti-parasite medication it was generally effect against those parasite in the past, after an Animal is treated with an anti-parasite drugs, the susceptible parasite die and the resistance paradise survive to pass on resistance genes to their offspring (parasite are often called worm and anti-parasite drug are often called dewormers).

### Factors contribute to Resistance anti parasite

- The biology of the parasite.
- Strength of the infected.
- The practices used to treat parasite.
- Properties of the particular anti-parasite used for treatment at any moment.
- Certain livestock management practices.

**Note:** Science shows that anti-parasite resistance however, this naturally resistance may be showed down.

### Resistance anti-malaria drug:

The emergency drug resistance parasite poses one of the greatest threats to malaria control and result in increased malaria morbidity and mortality. Artemisinin based combination therapies (ACTS) are recommended first line treatment for uncomplicated *P. falciparrum* malaria and are by must malaria endemic countries.

Therefore multiple drug resistance malaria recommended for use are e.g. Mefloquine, halofantrine and quinine with tetracycline, and also artesunate, atovaquone and proguanil is highly effective well tolerated treatment (Figure 5).

### Mosquito parasite

WHO about antimicrobial resistance world health organization agenda for antimicrobial resistance in human health prioritizes almost 40 research topic for evidence generation inform policy by 20230. It aims to guide policy makers researchers founders, to implementing partners industry civil society in generating new evidence to inform antimicrobial resistance policies and intervention as part of efforts to address antimicrobial resistance in the human health, especially infection cause by WHO bacteria pathogen and WHO fungal pathogen with critical importance for antimicrobial resistance such as candida auris and Drug resistance treatment of mycobacterium tuberculosis.

### Data analysis for antimicrobial resistance

Different regions area percentage of antimicrobial resistance mortality rate by 2050. By used region area of the worldwide and taken the percentage of the resistance of antimicrobial at the difference region areas worldwide that is in mortality rate by 2050, the region areas of the worldwide are below (Table 5):

- Asia
- Africa
- Europe
- Latin American
- North American



Figure 4: Structure of fungus.

Table 5: Table of mortality rate by 2050 AMR Region areas.

S/N	Region areas of AMR	Amount of resistance	% of resistance
1	ASIA	4,330,00	80%
2	AFRICA	4,150,00	75%
3	EUROPE	390,000	60%
4	LATIN AMERICAN	392,000	64%
5	NORTH AMERICAN	317,000	55%
6	OCEANIA	22,000	35%

- Ocenia

All these are part of the region that antimicrobial resistance, but any regions have different antimicrobial that highly resistance in their areas.

e.g **Asia:** Asia have issues of streptococcus pneumoniae have be found in Asia country, particularly erythromycin resistance increases dramatically many in Asian countries 75%.

**African:** African have issues of Ampicillin 84.5% and cotrimaxazole 68.5% among the Gram negative bacilli (30) Gram positive cocci show resistance to Nalidixic acid (81%) and with E. coli showing high as 84% resistance to ampicillin and 68% to Cotrimoxazole.

**Europe:** Escherichia coli resistance to major antibiotic is increases in almost all countries in Europe.

**Latin American:** Latin American has issues resistance of carbenem resistance according to the surveillance data from Latin American.

**North American:** by data pointed out that have issues of fluoroquinolone resistance of E.coli has be reported in 92 member state out of 194 and 5 out of 6 WHO global regions.

**Oceania:** according to the 2014 surveillance reported based on 2011/12 data, resistance of K pneumoniae isolated third generation cephalosporin in Kiribati was 1%, only one reported of carbapenem resistance was identified and in 0.7% isolated from hospital, also salmonella spp studied about typhoidal salmonella was from eastern Highland province 58%(22/38) of isolates were resistant to chloramphenicol, 37% (14/38) to kanamycin, 53% (20/38) ampicillin (Figure 6).



Figure 5: Mosquito parasite.

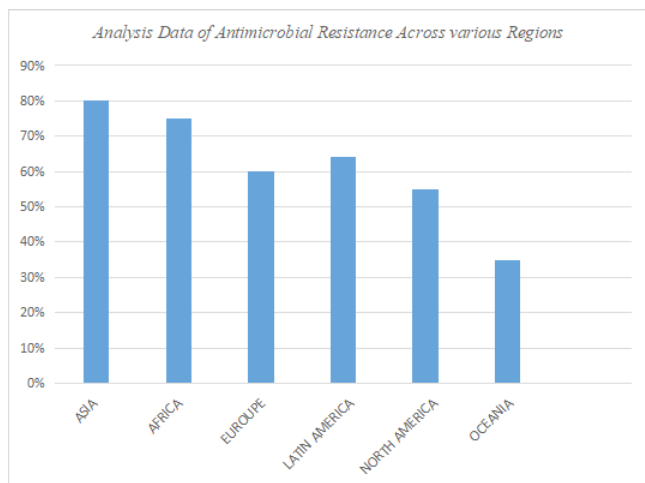


Figure 6: Analysis data of Antimicrobial Resistance.

### Control of AMR

- Use of antibiotic by a certified health professional.
- Never demand antibiotic if your health workers say you do not need them.
- Always follow your health workers advice when using antibiotics.
- Environmental hygiene.

### Prevention of Antimicrobial Resistance (AMR)

- Screening for diagnosis.
- Antibiotic prescribed by the patient required.
- Follow antibiotic guideline.
- Infection control e.g antiseptic, hand hygiene, use personal protective equipment and cleaning equipment room.
- Antibiotic come under schedule H so avoid use as OTC medicine.

### Conclusion

Make sure to control environmental sanitation and follow instruction of medical professional during prescription, also don taken any antibiotics without diagnosis that is proper investigation of actually pathological Diseases in the patient body, and avoid safe medication.

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