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ANTIBIOTIC MISUSE: A THREAT TO THE COMMUNITY

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ABSTRACT: Lack of awareness about antibiotics use among healthcare practitioners can be a great threat to the community. There is a need to bring awareness among the healthcare providers and the pharmacists regarding the over the counter (OTC) medications list and indications of OTC medication prescribing and dispensing. Pharmacists are important members of the healthcare team and they play a major role in medicine use and the provision of advice regarding appropriate medicines use. Education and training of pharmacists has the potential to influence the behavior of healthcare team members and consumers as part of a multidimensional strategy for changing practice and ensuring the quality use of antibiotics. They are well placed to improve the understanding of antibiotics and inform their judicious use by direct contact with consumers in the community and in hospitals. Consumer education is an important component of the fight against AMR and pharmacists can improve consumer's awareness of safe and appropriate medication practices concerning antibiotics. Interventions should encompass the enforcement of the policy of prohibiting the over-the-counter sale of antibiotics, the utilization of antimicrobial stewardship programmes, the active participation of clinicians in audits, the use of valid rapid point-of-care tests, the promotion of delayed antibiotic prescribing strategies, the enhancement of communication skills with patients with the help of data brochures and therefore the performance of more pragmatic studies in primary care with outcomes that are of clinicians' interest, like complications and clinical outcomes.

INTRODUCTION: Antibiotic misuse has become a common problem in the community. It is dangerously affecting the Antimicrobial Resistance (AMR) pattern as antibiotic misuse/overuse can lead to antimicrobial resistance and further can increase the susceptibility of various adverse drug reactions over time.

Antimicrobial resistance is a global public health challenge, which has been accelerated by the overuse of antibiotics worldwide. Increased antimicrobial resistance (AMR) is the cause of severe infections, complications, longer hospital stays and increased mortality [1].

Each drug or antibiotic has its own benefits and risks leading to adverse effects and therefore has to be used cautiously. Lack of awareness among physicians, Registered Medical Practitioners, nurses and other healthcare providers can be a huge threat to the community [2]. In recent years, the trends indicate this is more prominent in rural areas in comparison to the urban metropolitan

communities [3]. Illiteracy, language barriers, lack of knowledge about the medicine use, lack of counseling by the healthcare providers due to their busy time schedule could be one of the possible reasons leading to antibiotic misuse [4, 5]. There is a need to bring awareness among the healthcare providers and the pharmacists regarding the over-the-counter (OTC) medications list and indications of OTC medication prescribing and dispensing [4, 5]. Pharmacists are important members of the healthcare team and they play a major role in medicine use and the provision of advice regarding appropriate medicines use [6].

Education and training of pharmacists has the potential to influence the behavior of healthcare team members and consumers [7] as part of a multidimensional strategy for changing practice and ensuring the quality use of antibiotics [8]. They are well placed to improve the understanding of antibiotics and inform their judicious use by direct contact with consumers in the community [9] and in hospitals [10]. Consumer education is an important component of the fight against AMR and pharmacists can improve consumer's awareness of

safe and appropriate medication practices concerning antibiotics [11]. Here we present a similar case report providing insights into irrational use of antibiotics in healthcare settings.

Case Report: A 34-year-old male presented to the hospital in the department of gastroenterology with chief complaints of yellowish discoloration of sclera for 15 days, ethanolic+, dark urine+, LAI since 2 weeks back, 2 episodes of vomiting. The patient consulted a local physician. Before admission to our hospital and the following tests were done. This showed:

1. PT: 15.3 (11 to 14 seconds.)

2. INR: 1.3 (<1.3 seconds)

3. CRP: 11.1 (<10 mg/dL)

4. ESR: 15.1 mm/hr (0 to 22 mm/hr)

5. RBS: 79 mg/dL (80-130 mg/dL)

6. Liver function test reports before admission to the hospital are given in **Table 1.**

TABLE 1: LIVER FUNCTION TEST REPORTS BEFORE ADMISSION TO THE HOSPITAL

Lft Parameters	ReferenceRange	01/11/2022	03/11/2022	05/11/2022	09/11/2022
Total Bilirubin	0-0.2 mg/dL	15	17.5	20.4	27.9
ALT	0-40 U/L	1095	881	918	770
AST	0-50 U/L	3390	295	865	879
ALP	30-120 U/L	–	–	—	159

ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alanine phosphatase.

Patient had a history of non healing ulcer on right lateral malleolus, fever (1 episode) 15 days ago. The patient had no known comorbidities and no history of itching, weight loss, cough, loss of appetite, altered sensorium, malena, haematuria. The provisional diagnosis was made to be acute hepatitis. On medication history interview, the patient was taking Over the Counter (OTC) antibiotics after consulting a Registered Medical Practitioner (verbal-telephonic order) at his native place in Guntur and duration of administration was not mentioned. He was taking Inj. Monocef 1 gm IV Q24H, Inj. Lincomycin 600 mg IV Q24H, Inj. Ampoxin 1 gm IV Q24H, Tab Linezolid 600 mg P/O Q24h and continued OTC for 40 days without any medical advice. After which he developed jaundice and presented to our hospital. After admission, LFT, serum LDH, CBP, Anti-HAV

IgM, Anti HEV-IgM, RT-PCR, CUE, USG-abdomen and pelvis was Advised. Based on these parameters, the final diagnosis was confirmed as "Drug induced liver injury and Acute Hepatitis"

The Laboratory investigations which were done on Day 1 were as follows:

CBP: Normal, Anti-HAV IgM: Negative, Anti HEV-IgM: Negative (which ruled out Hepatitis A, Hepatitis E) AFP: 852.6 (H), ASMA: Negative (Ruled out autoimmune hepatitis), ANA: Negative, AMA: Negative. CMV DNA, Quantitative PCR: Negative. Herpes simplex virus: negative, Epstein Barr virus: negative. RFT was completely normal. Serum immunoglobulin IgG: 1698(H). GGTP: 1698 (H).

Lipid profile showed Low HDL: 29 mg/dL, High VLDL: 90 mg/dL, HBA1c: 5.5%. LFT reports showed hyperbilirubinemia and transaminitis as shown in **Table 2**.

TABLE 2: LIVER FUNCTION TEST REPORTS DURING THE HOSPITAL STAY

LFT Parameters Rs	Reference Range	Day 1	Day 3	Day 6	Day 13
Direct Bilirubin	0-0.2 mg/dL	13.1	12.7	12.4	6.7
Indirect Bilirubin	0.2-0.8 mg/dL	11.7	10.1	10.8	6.0
ALT	0-40 U/L	654	373	204	101
AST	0-50 U/L	514	273	187	120
ALP	30-120 U/L	142	104	106	96
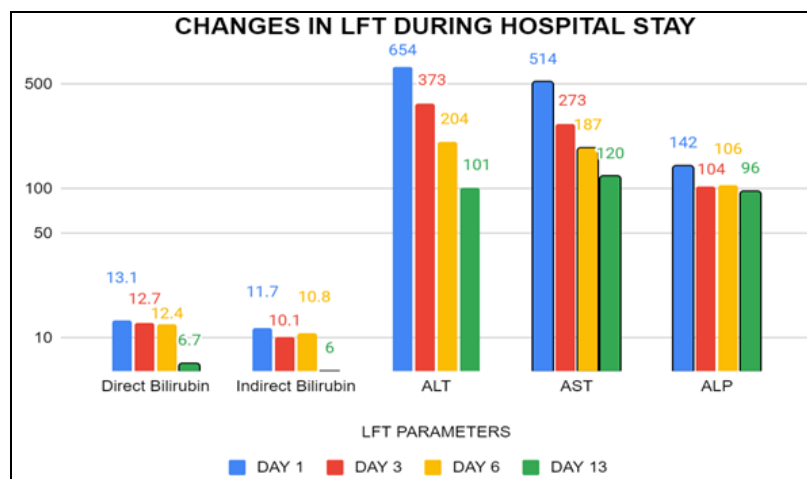
FIG. 1: CHANGES IN LFT DURING THE HOSPITAL STAY

Ultrasound abdomen with Splenoportal Doppler showed Grade 1 diffuse hepatic steatosis, contracted gallbladder with wall thickening and edema, normal splenoportal Doppler study. Triphasic MRI showed diffuse periportal edema, oedematous thickening of gallbladder, splenomegaly. Liver Biopsy of right lobe (segment VIII) for HPE showed Chronic active hepatitis with cholestatic rosette formation with mild cholestasis with focal ballooning with focal interface activity, portal to portal bridging by inflammation, mild portal and lobular mixed inflammation and interphase activity and mild portal fibrosis. Morphology favors: Drug induced hepatitis (cholestatic and hepatic pattern. During the course of hospital stay, patient was treated with IV fluids, Laxatives, N-Acetyl Cysteine infusion, PPI and other supportive medications (Tab. Ursodeoxycholic acid 300mg and Tab. Ademethionine 400mg p/o twice daily till follow up). The patient was discharged in a hemodynamically stable condition.

DISCUSSION: Antimicrobial resistance (AMR) is recognized collectively of the best threats to human health worldwide. Just one organism, Methicillin-Resistant *Staphylococcus aureus* (MRSA), kills more Americans each year than emphysema, HIV/AIDS, Parkinson's disease and homicide combined [12] Carbapenem resistant Enterobacteriaceae spp. and extended-spectrum beta- lactamase-producing Enterobacteriaceae are isolated in recent years.

The risk of ADRs has been high with the prolonged use of antibiotics. Parenteral administration of ceftriaxone has been associated with development of biliary sludge in 3% to 46% of patients. The incidence could also be higher in children than adults and is related to higher doses and longer courses of treatment and possibly with fasting or dehydration. The syndrome is observed as "pseudolithiasis" because the sludge and stones consist largely of ceftriaxone and that they resolve spontaneously when the drug is stopped, indicating that surgery will be avoided. Most cases occur usually with less or no symptoms. Ceftriaxone can also cause an immunoallergic type of cholestatic hepatitis just like what has been described with other cephalosporins. This reaction is idiosyncratic and is extremely rare. Symptoms of abdominal pain, nausea, pruritus and jaundice arise within 1 to 4 weeks of initiation of therapy and may worsen for 1 to 2 weeks after stopping the antibiotic which is

an evident in our case. A cholestatic pattern of serum enzyme elevations and immunoallergic features of fever, rash and eosinophilia are prevalent. The injury is sometimes mild and self-limited [13, 14, 15]. Ceftriaxone could be a very likely reason behind clinically apparent liver injury and may also result in biliary sludge and "pseudolithiasis" caused by crystallization of ceftriaxone in bile present within the gallbladder or biliary tree) [2].

Few cases of linezolid-induced lactic acidosis or severe drug-induced liver injury have been reported; therefore, these side effects may not be widely acceptable. Of the cases reported, most patients had used the antibiotic for a prolonged duration. These side effects of linezolid are therefore thought to be duration dependent, and it is recommended to limit its use to less than 28 days [27]. Prolonged Linezolid therapy cause hepatotoxicity, lactic acidosis; peripheral and optic neuropathy, and bone marrow suppression, but diabetic soft tissue infections, bone infections, and chronic infections required to prolong linezolid therapy [16, 17, 18]. Rare instances of idiosyncratic liver injury have been reported in persons receiving the aminopenicillins. The incidence is much lower with ampicillin than occurs with amoxicillin, occurring probably in less than 1 in 100,000 exposed persons [19]. Cases are characterized by a brief latency phase of some days to as long as two week [19].

There is no literature on lincomycin induced acute hepatitis. However, Clindamycin therapy has also been linked to a clinically apparent, idiosyncratic liver injury that arises between 1 to 3 weeks after starting either oral or parenteral therapy [20]. The cause of ALT elevations during high dose Clindamycin therapy is not known, but may be due to a direct but mild injury to the liver [21]. The Modified Hartwig and Siegel scale predicts the severity of ADR with the suspected drug. According to this scale, the patient had Level 4 ADR which is considered moderate risk for ADR.

TABLE 3: MODIFIED HARTWIG AND SIEGEL SCALE [22]

Level	Criteria
Mild (Level 1)	The ADR requires no change in the treatment with the suspected drug.
Mild (Level 2)	The ADR requires that the suspected drug be withheld, discontinued, or otherwise changed. No antidote or other treatment is required, and there is no increase in length of stay.
Moderate (Level 3)	The ADR requires that the suspected drug be withheld, discontinued, or otherwise changed, and/or an antidote or other treatment is required with no increase in length of stay.
Moderate (Level 4)	Any level 3 ADR that increases the length of stay by at least one day or The ADR is the reason for admission.
Severe (Level 5)	Any level 4 ADR that requires intensive medical care.
Severe (Level 6)	ADR causing permanent harm to the patient.
Severe (Level 7	The ADR either directly or indirectly leading to the death of the patient
ADR: Adverse Drug reaction	

Benefits of Antibiotics: Antibiotics haven't only saved numerous lives; they have played a pivotal role in achieving major advances in medicine and surgery.

They have successfully prevented or treated infections which will occur in patients who are receiving chemotherapy treatments; who have chronic diseases like diabetes, end-stage renal disease, or rheumatoid arthritis; or who have had complex surgeries like organ transplants, joint replacements, or cardiac surgery [23, 24]. Antibiotics have also helped to increase expected life spans by changing the result of bacterial infections [23]. In 1920, people within the U.S. were expected to live to be only 56.4 years old; now, however, the common U.S. life is nearly 80 years. Antibiotics have had similar beneficial effects globally. In developing countries where sanitation remains poor, antibiotics decrease the morbidity and mortality caused by food-borne and other poverty-related infections [24].

Strategies to Control AMR in Clinical Settings:

1. Prescribing fewer antibiotics is required in order to control antimicrobial resistance. The goal is to promote a rational use of antibiotics

by prescribing antibiotics only to patients who are expected to benefit from the treatment [1]. A reduction in antibiotic consumption results in a reduction of resistance.

2. Law enforcement to prohibit the illegal over-the-counter sale of antibiotics at pharmacies and the sale of antibiotics for humans and animals on the free market should be promoted worldwide.

3. Interventions should encompass the enforcement of the policy of prohibiting the over-the- counter sale of antibiotics, the utilization of antimicrobial stewardship programmes, the active participation of clinicians in audits, the use of valid rapid point-of-care tests, the promotion of delayed antibiotic prescribing strategies, the enhancement of communication skills with patients with the help of data brochures and therefore the performance of more pragmatic studies in primary care with outcomes that are of clinicians' interest, like complications and clinical outcomes [25, 26, 27].

CONCLUSION: In our report, it is evident that the use of OTC medications, especially the antibiotics, could lead to dangerous outcomes. The above-mentioned case is a case of both clinical negligence and patient misinterpretation. Lack of patient counseling, verbal drug order with incomplete information on the duration of the therapy, lack of follow up of the patient by the RMP and failure of conducting culture sensitivity test to order broad spectrum antibiotics are the factors associated with the irrational use of antibiotics. Pharmacists play a huge role in avoiding such errors by providing a communication link between the patient and the physician.

CONFLICT OF INTEREST: The authors declare no conflict of interest.

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