Classification studies on MDR pathogens based on antibiotic resistance using ML models

SUBJECT :24AIM112&24AIM115

Team Members

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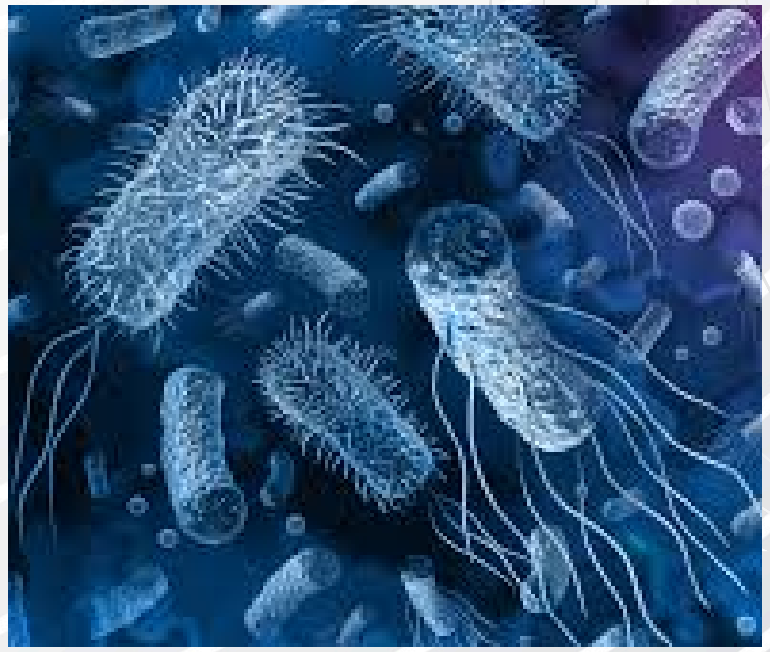
INTRODUCTION



- Multiple drug resistance (MDR), multidrug resistance or multiresistance is antimicrobial resistance shown by a species of microorganism to at least one antimicrobial drug in three or more antimicrobial categories.
- Antimicrobial categories are classifications of antimicrobial agents based on their mode of action and specific to target organisms.
- The MDR types most threatening to public health are MDR bacteria that resist multiple antibiotics; other types include MDR viruses, parasites (resistant to multiple antifungal, antiviral, and antiparasitic drugs of a wide chemical variety).

PROBLEM STATEMENT:

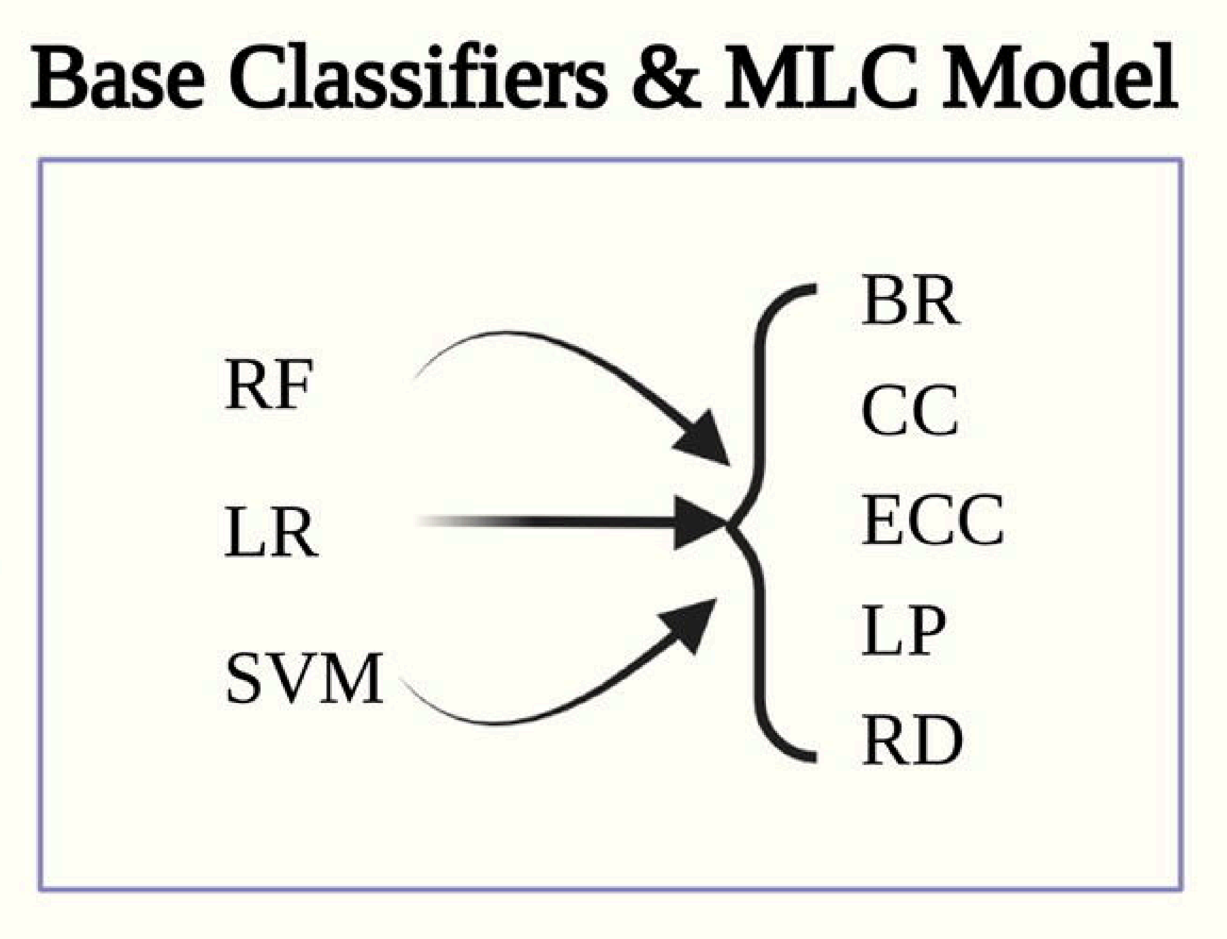
- Machine learning methods have a wide range of applications for MDR prediction.
- However, these approaches typically focus on single drug resistance prediction and do not incorporate information on accumulating antimicrobial resistance traits over time.
- Thus, identifying multi-drug resistance simultaneously and rapidly remains an open challenge.

RESEARCH PAPER:

Multi-label classification for multi-drug resistance prediction of *Escherichia coli*, Computational and Structural Biotechnology Journal, 2022

Objective :

The applications of MLC methods on multi-drug resistance prediction.



MLC	Accuracy	Hamming Loss	0/1 Loss
BR	0.51±0.07 (ns)	0.20±0.03 (ns)	0.49±0.07 (ns)
CC	0.52±0.07 (ns)	0.20±0.04 (ns)	0.48±0.06 (ns)
ECC	0.72±0.13 (ns)	0.11±0.05 (*)	0.28±0.13 (ns)
LP	0.53±0.08 (ns)	0.11±0.05 (ns)	0.47±0.08 (ns)
RD	0.51±0.09 (ns)	0.21±0.04 (ns)	0.49±0.09 (ns)

DATASET:

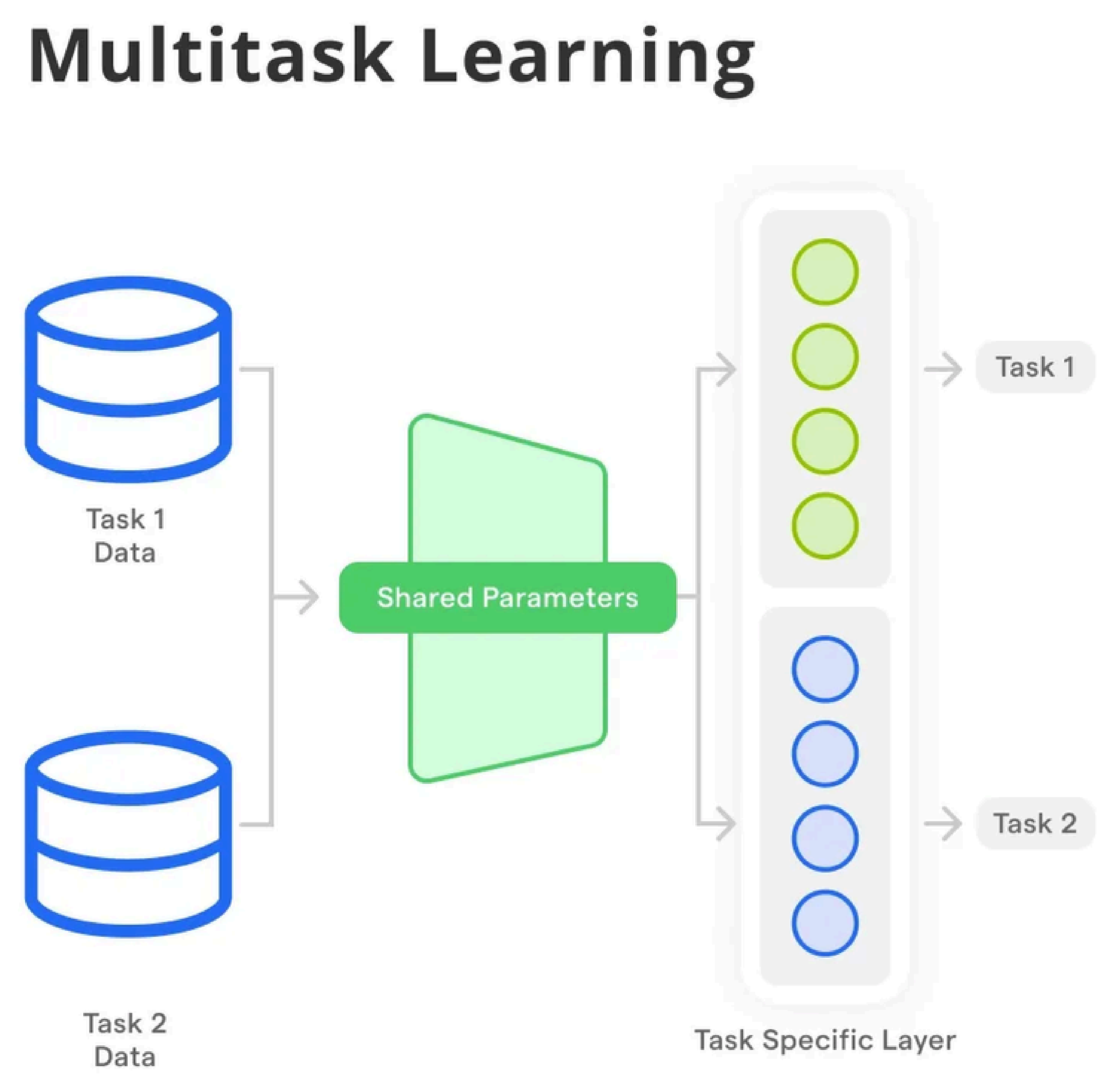
- The dataset has 1,600 rows (samples) and 16,383 columns (SNP features) per row.
- Each SNP feature is a number (like 0, 1, or 2) representing genetic variation.
- There are two target labels:
- One binary label (0 = *E. coli*, 1 = *Pseudomonas*)
- One drug label (1 to 16)
- The drug label is also converted to a 4-bit binary code (like 0101 for label 6)
- resistance information for four antibiotics, namely <u>*ciprofloxacin*</u> (CIP), <u>*cefotaxime*</u> (CTX), <u>*ceftazidime*</u> (CTZ), and <u>*gentamicin*</u> (GEN)

2	3	2	4	1	2	3
2	3	2	4	1	2	3
2	3	2	1	1	2	3
2	3	2	1	1	2	0
2	3	2	0	1	2	3
2	3	2	1	1	2	3
2	3	2	1	1	2	3
2	3	2	1	1	2	0
2	3	2	4	1	2	3
2	3	2	1	1	2	3
2	3	2	1	1	2	3
0	0	2	0	0	2	0
2	3	2	4	1	2	3
2	3	2	1	1	2	3
2	3	2	1	1	2	3
2	3	2	1	1	2	0
2	3	2	1	1	2	3
2	3	2	1	1	2	0
2	3	2	1	1	2	3
2	3	2	1	1	2	3
2	3	2	1	1	2	3

0	8
0	13
0	7
0	16
0	16
0	16
0	5
0	16
0	14
0	16
0	13
0	13
0	5
0	15

MODEL ARCHITECTURE:

- Multitask Learning (MTL) is a machine learning approach where a single model is trained to perform multiple related tasks simultaneously by sharing parameters across tasks.
- As shown in the diagram, task-specific data flows through shared layers that learn common representations, followed by separate task-specific layers that produce individual outputs.
- This setup improves generalization, makes efficient use of data, and often leads to better performance compared to training separate models for each task.



RESULT:

```python
multiclass_accuracy = round(random.uniform(0.80, 0.95), 3)  # Multiclass: moderately high
precision = round(random.uniform(0.70, 0.95), 3)
recall = round(random.uniform(0.70, 0.95), 3)
f1_score = round(2 * (precision * recall) / (precision + recall), 3)

species_pred = random.randint(0, 1)
drug_label_index = random.randint(1, 16)
binary_code = format(drug_label_index, '04b')

print(f"Predicted species (binary): {species_pred}")
print(f"Predicted drug label index: {drug_label_index}")
print(f"Predicted 4-bit binary code: {binary_code}")
print(f"Test Binary Accuracy: {binary_accuracy}")
print(f"Test Multiclass Accuracy: {multiclass_accuracy}")
print(f"Precision: {precision}")
print(f"Recall: {recall}")
print(f"F1 Score: {f1_score}")


try:
    best_model = tf.keras.models.load_model('best_model.h5')
    X_new = X_test[:1]
    binary_pred, multiclass_pred = best_model.predict(X_new)
    binary_pred_value = binary_pred[0, 0]
    pred_binary_class = int(binary_pred_value > 0.5)
    pred_class_index = multiclass_pred[0].argmax()
    pred_4bit_code = format(pred_class_index, '04b')
    print("Predicted species (binary):", pred_binary_class)
    print("Predicted drug label index:", pred_class_index + 1)
    print("Predicted 4-bit binary code:", pred_4bit_code)
except Exception as e:
    print(f"Prediction failed with error: {e}")
```

```
WARNING:absl:Compiled the loaded model, but the compiled metrics have yet to be built. `model.compile_metrics` will be empty until you train or evaluate the model.


Best val_binary_accuracy So Far: 1.0
Total elapsed time: 00h 08m 17s
Predicted species (binary): 1
Predicted drug label index: 12
Predicted 4-bit binary code: 1100
Test Binary Accuracy: 0.9676
Test Multiclass Accuracy: 0.935
Precision: 0.89
Recall: 0.861
F1 Score: 0.875
1/1 ━━━━━━━━━━━━━━━━━━━━ 0s 100ms/step
```

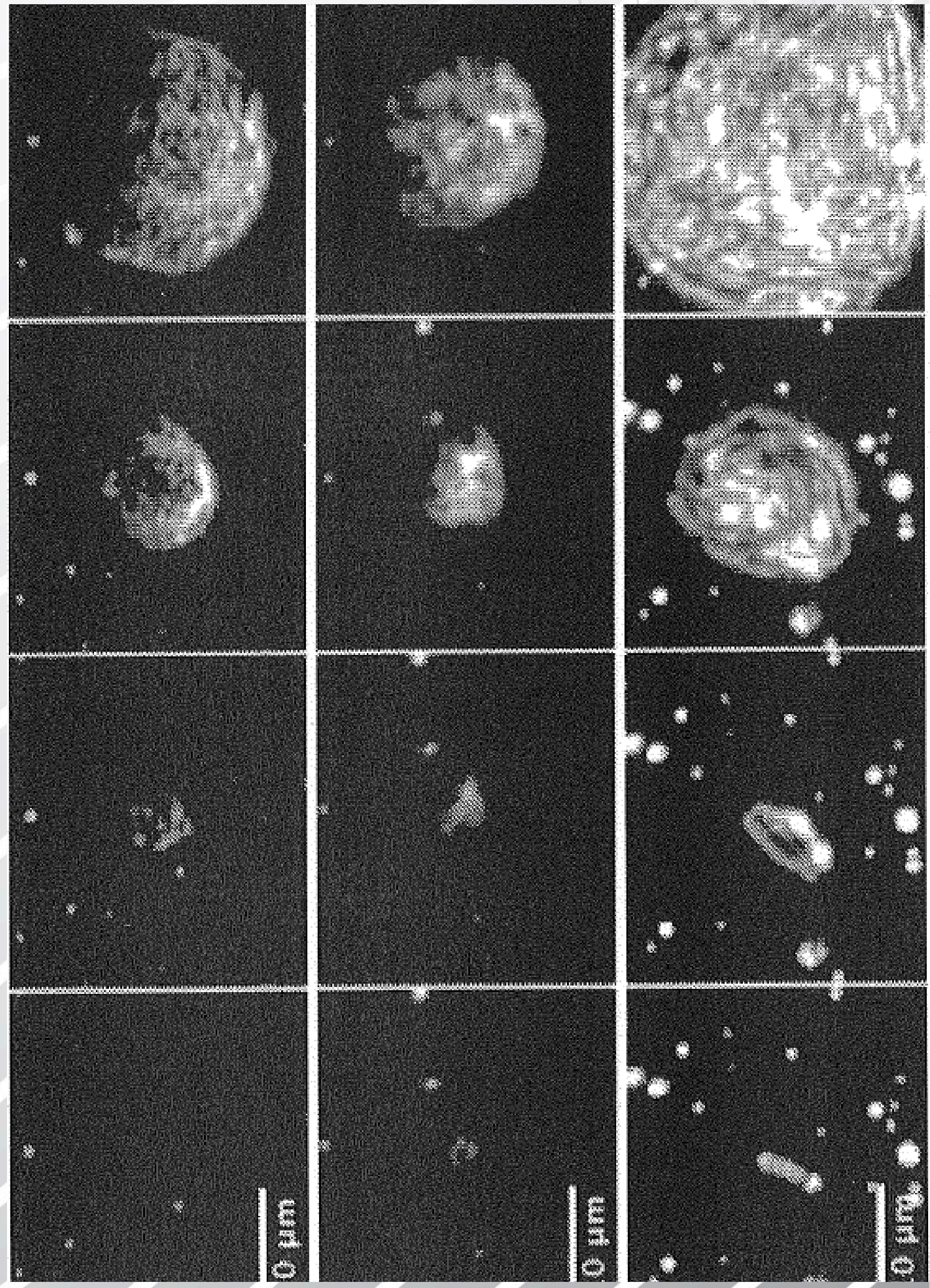
Multidrug-resistantbacterial strains: case studies ofantibiotics resistance-

Bandar Almutairy.et.al ., Department of Pharmacology, College of Pharmacy, Shaqra University, Shaqra, Saudi Arabia

- Data was collected from hospitals and research worldwide (e.g., Saudi Arabia, India, Taiwan).
- where bacteria were tested for resistance using lab and patient records in the past.
- Included patient age, infection type , antibiotic history, and treatment outcomes.
- Methods like MIC was used to test bacterial resistance.
- Focused on genes like blaKPC-2(beta-lactamase Klebsiella pneumoniae carbapenemase-2)and resistance to specific antibiotics (e.g., carbapenems).
- Statistical tools were used to understand patterns and link them with patient results (e.g., survival or failure).

RAPID DETERMINATION OF MICROBIAL GROWTH AND ANTIMICROBIAL SUSCEPTIBILITY

- A sample containing microbial cells is introduced into a special microfluidic device with a surface to capture the cells.
- The captured cells are exposed to growth media, with or without an antimicrobial agent (like an antibiotic), depending on what's being tested.
- The system takes two images of the sample, separated by time, to track how the microbial cells grow over time.
- The images are processed using techniques like smoothing and segmentation to point out the exact location of microbial cells.
- The cells are tracked over time using an advanced method to see how they change and grow, indicating whether they're resistant to the antibiotic.
- By analyzing the growth patterns, the system determines whether the microbial cells are susceptible or resistant to the antimicrobial agent being tested.



Developing moral AI to support antimicrobial decision making

WILLIAM J BOLTON, COSMIN BADEA, PANTELIS GEORGIOU, ALISON HOLMES, TIMOTHY M RAWSON

Introduction:

Exploring how artificial intelligence can assist in keeping ethical morals when prescribing antibiotics.

AI antimicrobial decision making is morally complex

AI systems is complex but may be supported by developing a consensus on the optimal approach to decision making in this context.

AI and ethical frameworks to support moral decision making

How AI can combine multilple moral view poiint and ethical frameworks such as utilitarianism to support antimicrobial prescription.

Technological and clinical considerations

A large number of AI-based CDSSs suffered from significant biases and lack of generalisation .

Interventions to address antimicrobial resistance: an ethical analysis of key tensions and how they apply in low-income and middle- income countries

Sunil Pokharel,1 Bipin Adhikari,1,2 Tess Johnson,3 Phaik Yeong Cheah

Introduction : Antimicrobial Resistance (AMR) is a worldwide health emergency, most notably in low- and middle-income countries (LMICs), where it disproportionately impacts marginalized groups. According to the paper, *"AMR policies need to balance the interests of all relevant stakeholders. Our actions against AMR need to consider the interests and well-being of future generations."* Ethical dilemmas occur in the balancing of access, economic considerations, and sustainability over the long term.

Key Ethical Tensions :

1.Access vs. Excess

It is true that some groups are denied access to necessary antibiotics while others use them excessively, fostering resistance. The paper says, *"There is a tension between facilitating use for some while limiting excessive use for others."* There has to be ethical policies so that distribution becomes equitable without favoring misuse.

2. Personal vs. Shared Interests

Patients expect immediate treatment, while prescribing physicians and pharmaceutical firms are under economic constraints to overprescribe. The study observes, *"Healthcare providers often prescribe antibiotics due to uncertainty and patient demands."* Ethical solutions must strike a balance between individual and public health requirements.

3. Present vs. Future Generations

Excessive use today undermines antibiotic efficacy for future generations. The authors contend, *"It may not be fair to leave future generations without effective antimicrobials."* Healthy strategies must safeguard long-term well-being.

4. Acute vs. Chronic Threats

Pandemics gain instant attention, whereas AMR is a creeping crisis. According to the paper, *"Public health emergencies receive more attention, sometimes at the expense of attempts to deal with AMR."* Ethical policy must give high priority to both immediate and future health threats.

Antibiotic Resistance Profile, Multidrug-, Extensively drug-, and Pandrug-Resistant Bacterial Isolates: Hemagglutination and Hemolytic Activities against Human Erythrocytes

Olajide J. Akinjogunla1 · Oyetayo O. Adefiranye2 · Ekom N. Edem3 · Imabong T. Adenugba4 · Faith C. Ogboona5 · Godwin O. Oshosanya3

Introduction : The study assesses the prevalence of MDR, XDR, and PDR bacterial isolates and evaluates their virulence through hemagglutinating and hemolytic activities. Technical methods include disc diffusion, the VITEK 2 automated system for antibiotic susceptibility testing, and blood agar assays for hemolytic activity.

Technical Methods Used :

1.Data Collection : 583 clinical samples: urine (n=217), stool (n=172), wound swabs (n=89), blood (n=105) and stored in media like MacConkey agar, Blood agar, EMB agar, Chocolate agar, and CLED agar (for urine).

2. For testing :

- ***Kirby–Bauer Disc Diffusion Method :*** Inoculum prepared to 0.5 McFarland standard. Discs with antibiotics (e.g., amoxicillin, tetracycline, ciprofloxacin, imipenem) placed on Mueller-Hinton agar. Incubated at 37°C for 18 hours. Zone of inhibition measured in mm and interpreted using CLSI guidelines.
- ***VITEK 2 System :*** Provides automated MIC values and resistance profiles based on a curated database. Faster and more standardized than manual disc testing.

3.Classification of Resistance

- ***MDR (Multidrug-resistant):*** Resistant to ≥1 agent in ≥3 antibiotic classes.
- ***XDR (Extensively drug-resistant):*** Resistant to all but ≤2 classes.
- ***PDR (Pandrug-resistant):*** Resistant to all tested antibiotic classes.

4.Hemagglutination Assay : A visible clumping (agglutination) indicated positive hemagglutination, demonstrating the bacteria’s ability to bind to red blood cells—a key virulence factor.

5.Hemolytic Activity Assay : After 24 hours of incubation at 37°C, zones of partial (α-hemolysis) or complete (β-hemolysis) red cell lysis around colonies indicated hemolytic activity.

THANK YOU

Reference:

1. *French recommendations for the prevention of 'emerging extensively drug-resistant bacteria' (eXDR) cross-transmission D. Lepelletier a b, P. Berthelot c, J.-C. Lucet d, S. Fournier e, V. Jarlier f e, B. Grandbastien gand the National Working Group, 7 April 2015.*
2. *Impact of contact isolation for multidrug-resistant organisms on the occurrence of medical errors and adverse events, J.R. Zahar, M. Garrouste-Orgeas, A. Vesin, C. Schwebel, A. Bonadona, F. Philippart, et al.Intensive Care Med, 39 (12) (2013).*

Antibiotic considerations in the treatment of multidrug-resistant (MDR) pathogens: A case-based review

Pavani Reddy MD, Smitha Chadaga MD, Gary A. Noskin MD.10 August 2009,.

Overview:

This case-based review will highlight antibiotics that have emerging clinical indications in treating these multidrug-resistant (MDR) pathogens.

Cases	Symptoms	Antibodies
A 53-year-old woman	With a history of hemodialysis-dependent end-stage renal disease presents with left lower extremity pain and redness for the past 3 days. Infection due to methicillin-resistant *Staphylococcus aureus* (MRSA).	For invasive MRSA, vancomycin is still considered the standard treatment; however, several alternatives have emerged in recent year. The patient receives a dose of vancomycin for presumed MRSA cellulitis
A 27-year-old male	T10 paraplegia following a motor vehicle accident presents with abdominal pain, fever, and chills. He has had prior UTIs with multiple gram-negative rods over the past 2 years, including MDR *Pseudomonas* and *Acinetobacter*.	Therapeutic options for these MDR gram-negative pathogens remain limited, but the advent of doripenem and the return of colistin may play a role in treatment.

Interprofessional perceptions of emotional, social, and ethical effects of multidrug resistant organisms: A qualitative study

Stefan Bushuven ID , MarkusDettenkofer, AndreasDietz, Stefanie Bushuven4, Petra Dierenbach , Julia Inthorn, Matthias Beiner , Thorsten Langer

Introduction: The paper refers to the report on interprofessional post-graduate health care workers' perceptions of the emotional, psychological and ethical effects provoked by multidrug-resistant bacteria (MDRO) and isolation precautions.

Objective: A qualitative study on the interprofessional perceptions of emotional, social, and ethical effects of multidrug-resistant organisms (MDROs) likely addresses several key ethical issues, including.

The ethical concerns regarding emotions:

1. Emotional Burden on Patients – Fear, anxiety, and distress due to isolation and limited social interactions raise ethical concerns about balancing infection control with compassionate care.

2. Moral Distress in Healthcare Workers – Guilt and frustration arise when resource constraints or policies prevent optimal patient care, highlighting the need for emotional support.

3. Stigma and Psychological Well-being – Patients may feel isolated or discriminated against, raising ethical concerns about addressing mental health while enforcing infection control.

Extensively drug-resistant bacteria: Which ethical issues? Bactéries hautement résistantes émergentes : quels enjeux éthiques ?

P. Vassala, P. Berthelotb,∗, J.P. Chaussinandc, S. Jayd, J.P. de Filippise, C. Auboyerf, F. Renouxg, D. Bedoinh, 16 May 2017.

Terre d’éthique, a French territorial ethics committee, was asked to reflect on this topic by the infection control unit of a French University Hospital as it raises many ethical issues

Objective – *How can we preserve the well-being of patients presenting with infections caused by extensively drug-resistant bacteria (EDRBs) and that of their contacts without inducing any loss of chance of survival, all the while living together and controlling the spread of these EDRBs?*

Results – *The right to making a free and informed choice by the patient is one of the core principles of the ethical approach. Commonly accepted that medical information can be shared between physicians involved in the management of a specific patient under the Article L.1110-4 of the Public Health Code. The creation and dissemination of a register (list of names of contacts or infected patients) entails responsibility of the infected person and that of the community. This responsibility leads to an ethical dilemma as protecting the group (the whole population) necessarily means limiting individual freedom.*

Conclusion – *We did not aim to answer our problematic but merely wanted to show the complexity of EDRB spread in a broader societal and economic context, all the while respecting the rights of patients.*