Sultan Qaboos University
Research Department
Research Proposal (SQU)

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EXPECTED PROJECT DURATION:

Two years

GRANT REQUESTED (RO)

Total: 7,000

Year 1: 3,400	Year 2: 3,600

TITLE

An inquiry into the virulence, antimicrobial resistance genes, and susceptibility to newer antimicrobials of extremely and pan drug-resistant Gram-Negative Bacilli isolated from urinary tract infections.

SHORT TITLE: Virulence, antimicrobial resistance genes, and susceptibility to newer antimicrobials of resistant bacteria causing urinary tract infections

KEY WORDS

Virulence genes, antimicrobial resistance genes, UTI. XDR, PDR

THEMES *(Environmental and Biological, Energy and Non-renewable Resources, Life and Health Sciences, Humanities and Social Sciences, Information and Communication Systems, Fundamental, Materials, Educational, Industry-related)*

Life and Health Sciences

EXPECTED BENEFICIARIES

The results of this study will directly benefit UTI patients (cases of cystitis, pyelonephritis, and urosepsis) infected with extremely drug resistant (XDR) and pan drug resistant (PDR) Gram-negative bacilli by furthering, the knowledge about virulence factors and synergistic combinations of antibiotics that spare the newly introduced drugs, which can then be safeguarded to manage more invasive infections.

SUMMARY

A.

OUTLINE OF PROPOSED RESEARCH

Proposed research outline must include at least the following sub-sections:

1. INTRODUCTION

Urinary tract infections (UTIs) are among the most frequent infections in clinical practice worldwide requiring a considerable number of antibiotic prescriptions. It is a common complaint among patients presenting to General Practitioners, Family Medicine, Emergency Medicine, Medicine, Surgery, Obstetrics & Gynaecology and Paediatrics. About 60% of women and 12% of men will have at least one UTI during their lifetime, thus accounting for a significant burden of empiric antibiotic usage worldwide. [4]

The rapid pace of emergence of extended spectrum beta-lactamase producing organisms (ESBL), AmpC and carbapenem resistant organisms has made it difficult for the clinicians to keep up to date with the resistance patterns. [5-7]

Prescribing effective empiric antibiotic therapy can be quite a challenging task in these days of escalating AMR often leading to inappropriate antimicrobial use.[8] A rigorous study of epidemiology, demographics, etiology, antimicrobial resistance, virulence, and evaluation of newer drugs by the Microbiology Department is the need of the hour to enable appropriate antimicrobial prescribing and optimal patient care.

UTIs are caused predominantly by the extraintestinal *Escherichia coli* commonly known as uropathogenic *E. coli* (UPEC). [9] *E. coli* fall into four major phylogenetic groups; A, B1, B2 and D. [10] Clermont et al have described a simpler phylogenetic analysis which targets three genetic markers *chuA* (required for haeme transport), *yjaA* (unknown function) genes and a DNA fragment TSPE4.C2 [11] The majority of virulent *E. coli* strains belong to phylogenetic groups B2 and D as described by Johnson and Stell. [12] The major circulating UPEC clone, ST 131 is replete with toxins, adhesins, toxins and siderophores which aid in overcoming host defences. [13] Intimin like adhesins binds to the bladder epithelial cell lining. [14] Cytotoxic necrotizing and haemolytic factors assist in both spread and persistence of bacteria in the urinary tract.

The galloping antimicrobial resistance of UPEC strains is a grave public health concern. The strains are becoming more adept at acquiring resistance to antimicrobials through mobile genetic elements like plasmids, transposons and integrons.

While a large number of studies have focused on *E. coli* there is a paucity of similar studies on other uropathogens like *Klebsiella pneumoniae*, Tribe Proteae, *Pseudomomas aeruginosa, E. faecalis* and *Staphylococcus aureus* and *S. saprophyticus*.

Few studies have characterized the virulence properties and antibiotic resistance of uropathogens associated with UTIs in adults and children from the Middle East. In this study, we will investigate the prevalence of virulence genes, antimicrobial resistance and phylogenetic groups of pathogens isolated from patients with UTIs, along with assessment of newer drugs against XDR and PDR Gram negative bacilli isolated from UTI.

1.1. LITERATURE REVIEW

Antimicrobial resistance (AMR) is being increasingly referred to as "the silent tsunami facing modern medicine". [15] This unprecedented upsurge in AMR is breeding a new generation of 'superbug microbes' that are virtually untreatable with the existing antimicrobials. [16] AMR has become a grave global public health challenge partly due to a lack of newly developed antibiotics and an over reliance on existing drugs. According to the World Health Organization (WHO) this may lead to a global catastrophe leaving many people harmed or dying from simple infections that have become complicated (WHO, Antimicrobial Resistance, 2017). [17] The impacts of burgeoning antimicrobial resistance are wide ranging and costly, not only financially, but also in terms of global health, food sustainability and security, environmental wellbeing, and socio-economic development.[18]
AMR infections are estimated to cause 700,000 deaths each year globally. [19] O'Neill (2016) have found that due to the rising drug resistance for pathogens it is estimated that the burden of deaths from AMR could balloon to 10 million lives each year by 2050. O'Neill (2016) claimed that on this basis, by 2050, the death could be one person every three seconds. [20]

The emergence of the family of carbapenemase enzymes such as KPC, NDM-1, IMP, VIM, OXA-48 is undoubtedly one of the most significant health challenges of the century. Carbapenem resistant organisms (CRO) are usually hospital acquired pathogens and are associated with high mortality (>60%) and morbidity as published in many studies [9, 10]. Mechanisms of carbapenem resistance are heterogeneous. It can be mediated by carbapenemase production or via production of extended-spectrum β-lactamases (ESBLs) and/or AmpC cephalosporinases (AmpC) combined with altered membrane permeability (non-CP-CRE.[21] CRO are an increasing concern worldwide. The risk factors for CRO comes from KPC variants, the zinc-dependent metallo beta-lactamases (VIM, IMP, and NDM types) and OXA like (OXA-48, OXA 181, OXA-232, OXA-23) which inactivate many clinically relevant beta lactams.[22] Moreover, CRO show resistance to many important antibiotics, such as aminoglycosides and fluoroquinolones. [22]
OXA-48 is the predominant genotype circulating in Oman. The bacteria of greatest concern here is XDR and PDR *Escherichia coli*. Invasive blood stream infections caused by this and by other Gram negative bacteria subsequent to pyelonephritis and urosepsis are associated with high mortality rates. The emergence of carbapenemases and colistin resistance in Gram negative bacilli has caused global concern among the scientific, medical and public health communities. Both the CDC and the WHO consider carbapenem-resistant Enterobacterales (CRE) to constitute a significant threat that necessitates immediate action. [23,24.]
The treatment of choice in such extremely and pan drug resistant organisms is usually colistin. With the newer antimicrobials (cefiderocol, eravacyline and plazomycin) not yet available in our part of the world, we are reaching the end of the road as far as the treatment of Gram negative bacteria is concerned as colistin resistance is increasing fast. It is essential to assess the feasibility of these new antibiotics, alone and in combination to treat carbapenem and colistin resistant bacteria. Clinical data from prospective, randomized trials are lacking for combination therapy for carbapenem resistant Gram negative bacteria (CRGNB); however, *in-vitro* studies and accumulated retrospective experience suggest that combination therapy, including a carbapenem (eg, polymyxin-carbapenem or aminoglycoside-carbapenem), may have a mortality benefit in both CRGNB and Colistin resistant (CoR) bacteria. [3] Since resistance determinants vary from region to region, a proactive approach exploring effective antimicrobial therapy alone and in combinations by in vitro synergy should take place at local, regional, national and international levels to facilitate effective patient management.

In this study, we will evaluate the in-vitro effectiveness of various combinations of colistin and carbapenem with the new antimicrobial agents against CRGNB and CoR clinical isolates of Gram negative bacilli using the checkerboard, time-kill and Etest assays. Whole genome sequence (WGS) analysis will shed light on the predominant multilocus sequence types circulating in this region and their resistance determinants. This analysis will also shed light on the bacterial determinants which enable antimicrobials to attain synergy-this to the best of

our knowledge is the first study of its kind in the world. WGS will enable us to study a large number of resistance determinants like colistin resistance, carbapenem resistance and fluoroquinolone resistance.

Characterization of antibiotic resistance determinants at the genomic level will play a critical role in understanding and potentially controlling the spread of pan drug -resistant (PDR) pathogens. Of particular concern in not only Oman but worldwide is the spread of pan drug resistant strains of *Klebsiella pneumoniae, Escherichia coli, Acinetobacter baumanii and Pseudomonas aeruginosa*. The circulating clonal types of these bacteria will be identified, their movement traced within the hospital. This will help to initiate control and preventive measures.
Thus, this study will shed light on clinical profile, virulence, resistance markers, dominant MLST types, phylogenetic groups, and synergistic antimicrobial combinations. These will go a long way in optimising patient management and instituting effective infection control policies in the hospital.

2. OBJECTIVES

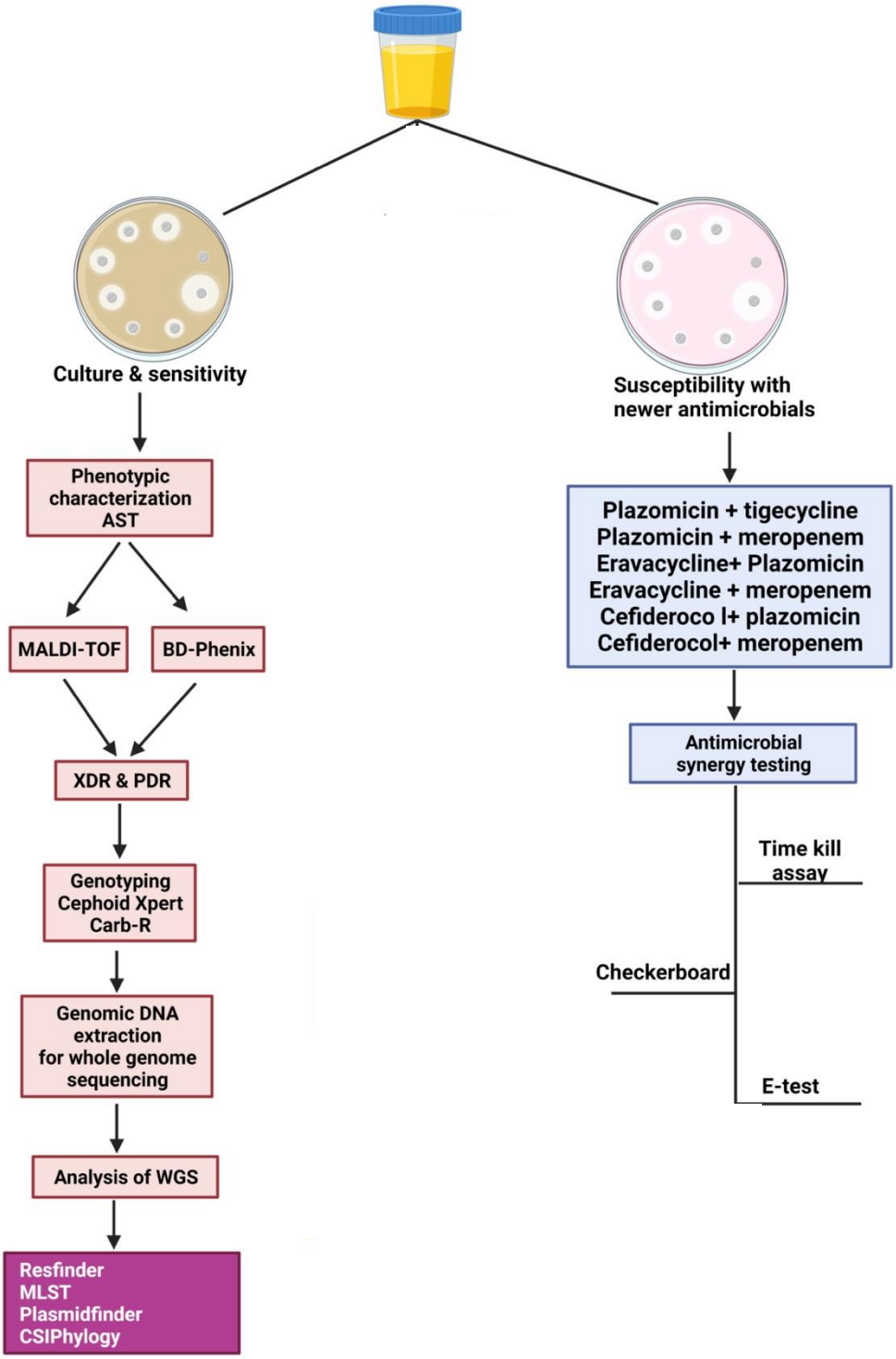
1) To assess risk factors, antimicrobial treatment and outcome of patients infected with Carbapenem resistant Gram negative bacilli (XDR) and colistin resistant Gram negative bacilli (PDR).
2) To study the whole genome sequenced strains of the predominant XDR and PDR GNB and identify their resistome, tolerome related genes along with virulence genes.
3) To assess *in-vitro* and *in-vivo* synergy of the different antimicrobial combinations using newer antimicrobial agents as the cornerstone drug in inhibiting the whole genome-sequenced representative strains of XDR and PDR Gram negative bacilli.
4) To study clonal relatedness between XDR and PDR Gram negative bacilli isolated from patients admitted in different wards of SQUH by whole genome sequencing of representative strains.

3. METHODOLOGY

This study will be conducted in the Department of Microbiology and Immunology in the Sultan Qaboos University (SQU), Muscat, Oman.
3.1 Study duration: January 2024 to January 2026.
3.2 Study Design: Prospective
3.3 Sample size: The sample size will be measured as follows: prevalence of antimicrobial resistance in Gram negative bacilli in Oman ranges from 17.3% to 37.6%. Considering prevalence as 30% and level of confidence as 95%, with an error margin of 5%, on either side of the estimate, the population size was 2000 with positivity as 30% the optimum sample size for the study was obtained as 273 (Raosoft calculator and Wayne et al, 7th ed). We however plan to include a minimum 330 Gram negative bacilli for our study. Raosoft calculator was used for calculating the sample size. http://www.raosoft.com/samplesize.html
3.4 Study Group
Consecutive UTI patients infected with XDR and PDR Gram negative bacilli will be recruited in the study. Demographic and clinical outcome data will be collected from the patient's electronic medical record.
3.5 Risk factors for acquiring XDR and PDR Gram negative bacilli:
The risk factors will include age, sex, status at culture collection, microbiologic data, antibiotics administered, treatment duration and site of infection. The risk factors will be collected from the patient's electronic medical record.
3.6 Collection and processing of samples
Appropriate urine samples (mid-stream, clean catch samples, catheter samples, percutaneous nephrostomy, suprapubic catheter, suprapubic aspirate etc) will be collected with proper aseptic precautions and transported rapidly in cool storage boxes (4^{o}C) to the microbiology

laboratory for analysis. One aliquot will be separated for routine culture and sensitivity. All samples will be processed according to the Clinical and Laboratory Standards Institute guideline (CLSI 2020) [29] using the routine semi-quantitative culture method . [30] Phenotypic characterization will initially be performed by MALDI-TOF (Bruker diagnostics) and BD Phoenix automated system (Becton Dickinson Diagnostic systems, Spark, MD, USA) XDR and PDR isolates will be characterised genotypically to carbapenemase level by Cepheid Xpert Carba-R assay (Cepheid, Sunnyvale, CA, USA). Antimicrobial susceptibility testing will be performed by Phoenix automated system as per CLSI2020, M100 30th ed.
All strains will be preserved and stored at -40^{o}C in sterile CryoBeads (Mast Diagnostics, UK) till further analysis.

3.7 Methodology at a glance:



Detailed Methodology

3.8.1 Genomic DNA Extraction for Whole genome sequencing:

Bacterial genome sequencing will be performed using the Ion Torrent PGM (Life Technologies, Carlsbad, CA) at Central Public Health laboratory. The bacterial genomic DNA will be extracted from pure bacterial cultures grown overnight on non-selective media. DSP Virus/Pathogen Mini Kit (Qiagen) will be used on automated nucleic extractor (QIAsymphony SP/AS, Qiagen) for extracting DNA. The concentration and purity of DNA will be checked using Qubit Fluorometric Quantification (Thermo).

3.8.2 Analysis of WGS data

The obtained sequence data will be analyzed using the freely available bioinformatics tools in the Centre for Genomic Epidemiology website. ResFinder, MLST, PlasmidFinder and CSIPhylogeny tools will be used to investigate the acquired antimicrobial resistance genes, multilocus sequence typing (MLST), plasmids and bacterial relatedness respectively. The CSIPhylogeny tool identifies the variations between the obtained sequence data (FASTA files) by identifying or calling and filtering high-quality SNPs (z-score higher than 1.96 for all SNPs) and eventually forming a phylogenetic tree using FastTree algorithm. In addition, the CARD bioinformatics website will be used to look for the resistance genes and their mechanisms of action.

3.8.3 Identification of virulence genes and antibiotic resistance genes

BLAST will be used to align denovo assembled genome sequences against the NCBI Bacterial Antimicrobial Resistance Reference Gene Database (http://www.ncbi.nlm.nih.gov/bioproject/PRJNA313047),ResFinder (http://www.genomicepidemiology.org70), and the Pasteur database of virulence genes (http://bigsdb.pasteur.fr/klebsiella/klebsiella.html). Antibiotic resistance genes investigated included carbapenemases and other ß-lactamase genes.

3.8.4 Molecular Typing by MLST

The MLST database at the Center of Genomic Epidemiology will be used to identify the sequence types (ST) of the study isolates using WGS data (https://cge.cbs.dtu.dk/services/MLST/).

eBURST

The program eBURST v 3.0 will be used to identify clonal complexes.

3.9 Susceptibility to newer antimicrobial agents

The susceptibilities of isolated strains to new antibiotics will be performed by determining the minimum inhibitory concentration (MIC) using microbroth dilution techniques (CLSI guideline) [30] This study aims to evaluate the efficacy of the following antimicrobial agents: Fosfomycin, colistin, doripenem, tigecycline, plazomicin, ceftolazane + tazobactam, ceftaroline + avibactam, meropenem + vaborbactam, ceftazidime + avibactam, eravacycline, cefiderocol by E tests (Liofilchem and Biomerieux)

The antimicrobial combinations which will be tested for synergy are the following

Plazomicin+tigecycline
Plazomycin+meropenem
Eravacycline+Plazomicin
Eravacycline + meropenem
Cefiderocol+plazomicin
Cefiderocol+ meropenem

3.10 Antimicrobial synergy testing

The in vitro synergistic bactericidal effects of the selected antibiotics against XDR and PDR strains will be assessed by Time kill assay, Checkerboard assay and E-test.

3.10.1 Time kill Assay (TKA)

Time kill Assay (TKA) will be performed using 96-well microtiter plate according to a published technique. [31]Antimicrobials will be tested alone and in combination with concentrations ranging from 1, 0.5, 0.25. MICs will be selected along with other ratios based on checkerboard results. Control experiments without antimicrobial agents will be conducted simultaneously with the TK assay.

The vials containing cation-adjusted Mueller-Hinton broth, antimicrobials, and the tested organisms at an initial density of 10^6 CFU/ml (10 ml volume) will be incubated at 35 ± 2 °C in ambient air. Aliquots will be removed at times 0, 6, and 24 h and serially diluted in 0.85% sodium chloride solution and plated on Mueller-Hinton agar plates for viable-colony counting.

Time-kill curve will be created by plotting bacterial cell counts for control, antibiotic alone or in combination with other antibiotics over estimated time. Results will be interpreted as follow:

- **Synergy:** if a reduction in colony count by ≥ 2 $\log_{10}$ CFU/ml at 6 or 24 h occurs compared with the most active single agent

Addition

- **Antagonism**: if an increase of ≥ 2 $\log_{10}$ CFU/ml occurs in the combination versus the most active single agent.
- **Indifference:** if an increase or decrease of < 2 log10 in colony counting with an antibiotic combination versus individual antimicrobials.
- **Additivity**: If FICI > 0.5 to ≤1

3.10.2 Checkerboard Assay (CB)

Broth microdilution checkerboard technique (BMC) will be performed to assess MICs of single or of combined antibiotics as recommended by CLSI.

The interactions will then calculate by using the formula:

§ **FICI= FICA+FICB** ,where:

- FICI = Fractional Inhibitory Concentration Index
- FICA = MIC_A in combination/ MIC_A alone
- FICA = MIC_B in combination/ MIC_B alone

FICI will be interpreted as follows:

- **Synergy**: If FICI 0.5
- **Partial synergism**: If FICI > 0.5 to <1 [3]
- **Indifference**: If FICI ≥ 1 to 4
- **Antagonism** : If FICI > 4

3.10.3 E-test methods

Minimum inhibitory concentration value of assayed antibiotics will be tested against all isolates using an E-test (BioMérieux, France). E-tests will be performed and interpreted according to the manufacturer's instructions. The Synergy testing will be performed in three different methods:

I) Method 1 Method (Cross Methods)

Mueller-Hinton agar (MHA) plate is inoculated with 0.5 McFarland matched inoculum, to which *E*-test strips are placed one over the other at 90° angle crossing at the MICs of the individual agent of the organism determined earlier. After incubation for 18 h, the zone of inhibition is read.

II) Method 2 (Fixed ratio methods)

Bacterial suspensions of investigated isolates with turbidity of 0.5 McFarland units will be inoculate in MHA (Mueller Hinton Agar) (150 mm diameter). MICs of drug A and Drug B will be performed along with the combination setup. For the combination setups, E-test strips containing the study antibiotics will be added to the bacterial lawn sequentially; the first E-

test strips (strip A) will be incubated for 1 hr at room temperature, then removed and saved as MIC_A reading. The second E-test strips (strip B) will be added immediately over the imprint of the E-test strips A. Plates will be incubated for 18 hrs at 35° C. Respective MIC strips/scales will be used for MICs reading by placing them in each gradient's position.

III) Method 3 (*E*-test MIC: MIC method)

In this method, one test strip is placed on the inoculated MHA plate and incubated at room temperature for 1 h to allow diffusion of the agent. After 1 h, the agar is marked adjacent to the previously determined MIC of the agent and removed. The second *E*-test strip is then placed over the imprint of the previous strip such that the mark on the agar corresponds to the MIC of the second agen . The resulting ellipse of inhibition is read after 20 h of incubation at 37°C.

Fractional inhibitory concentration index (FICI) will be calculated to assess synergistic activity in both methods by using the following formula:

§ **FICI= FICA+FICB**,where:

- FICI = Fractional Inhibitory Concentration Index
- FICA = MIC_A in combination/ MIC_A alone
- FICA = MIC_B in combination/ MIC_B alone

FICI interpretation will be as follows:

- **Synergy** : If FICI 0.5
- **Additivity** : If FICI > 0.5 to ≤1
- **Indifference** : If FICI ≥ 1 to 4
- **Antagonism** : If FICI > 4.[32]

3.12 Statistical analysis

A database of all clinical and other relevant details with real-time data entry will be created in Microsoft Excel (Office 2019 Professional for Windows; Microsoft). The statistical analysis will be performed using IBM Statistical Package for the Social Sciences (SPSS) Statistics for Windows [version 23.0, Professional] (IBM Corp., Armonk, N.Y., USA). The normality of the data will be analyzed through the Shapiro-Wilk test. For continuous variables, descriptive statistics will be used. Categorical variables will be reported as frequencies and percentages and appropriate statistical tests will be employed. Comparison of quantitative data between variables will be done using 2 tailed paired t-test. Results will be graphically represented and demonstrated.

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4. SIGNIFICANCE

Antibiotic resistance has been referred to as *"the silent tsunami facing modern medicine"*. Along with the rest of the Middle-east, Oman is also facing this unprecedented crisis in healthcare. With the exponential rise of antimicrobial resistance, it is important to map the resistance locally, nationally, and regionally to understand which antimicrobials are effective and which new antimicrobials should be introduced in the national therapeutic formulary for optimal patient management. Effective combination antimicrobial therapies may soon be the only treatment option available. Therefore, it is essential to identify the synergistic antimicrobial combinations that would play a pivotal role in reducing patient morbidity, mortality and length of stay in the hospital. This will be the first study emanating from Oman, which will focus on new synergistic antimicrobial combinations against not only the predominant OXA 48 gene producing CRGNB but also NDM, KPC, VIM, IMP and colistin- resistant GNB (*phoPQ, pmr AB, mgrB* mutations and *mcr* A and B genes)

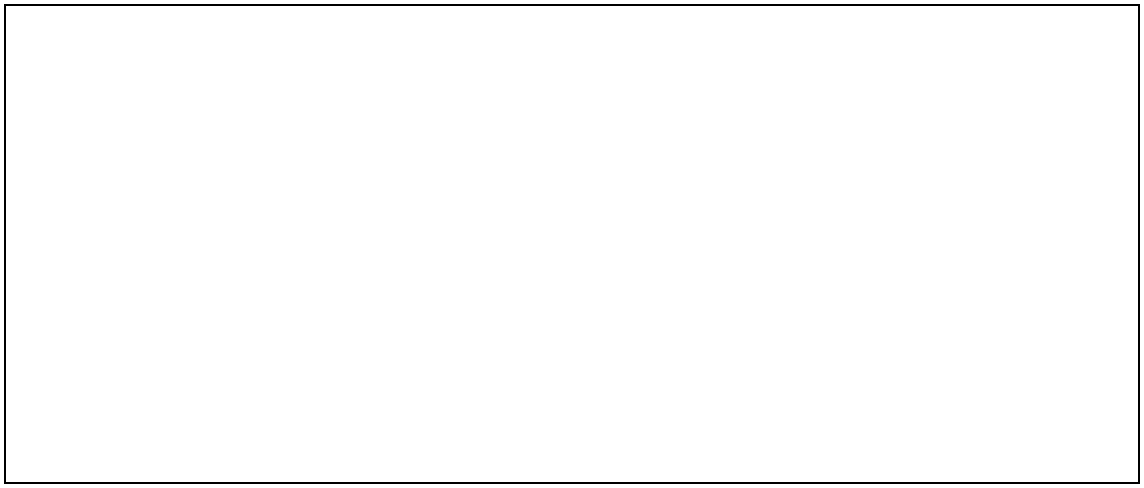
5. OUTCOME OF THE STUDY AND HOW IT WILL BENEFIT SQUH

This study will assess efficacy of newer antimicrobials as well as identify synergistic combinations to treat extremely and pan drug resistant Gram negative bacilli causing urinary tract infections. The knowledge emanating from this study will go a long way in guiding clinicians to prescribe the appropriate antimicrobials- whether they should resort to new drugs or use combination of drugs. If combination of drugs is opted for, then the results of this study will guide in selection of the correct combination which is likely to have synergistic outcome. This will undoubtedly lead to more effective patient care. The circulating MLST clonal types and phylogenetic groups of these bacteria will be identified and their movement traced within the hospital. This will help to initiate effective infection control and preventive measures not only in SQUH but also in the community.

	2024				2025				2026
	Jan-Mar	Apr-Jun	Jul-Aug	Sep-Dec	Jan-Mar	Apr-Jun	Jul-Aug	Sep-Dec	Jan
A									
B									
C									
E									
F									

6. TIMELINE/ DELIVERABLES

A	Samples collection
B	Ordering of consumables items
C	Data Collection and analysis: Continuous process
D	Performance of MIC, Synergy testing for carbapenem resistant Gram negative bacilli (XDR): from 12 months onwards: 1-2 publications
E	Performance of MIC, Synergy testing for colistin and fosfomycin resistant Gram negative bacilli (PDR): from next year onwards: 1-2 publications



DISSEMINATION PLAN (The plan is based on the researcher's expectations within 5 years of being awarded the grant)

7. Expected Intellectual Property (IP)

Expected Type of IP*	Description
Example: (Patents, process, machine, composition of matter, article of manufacture, copyright, know-how, new devices, chemical compound, etc.)	

* *Please refer to point (2.5) in SQU IP Policy*

8. EXPECTED PUBLICATIONS

Type of Publication	Number of Publications
Journal Paper	1-2
Conference Paper	1-2
Book Chapter	
Book	
Other (please specify)	

9. ORGANIZATION OF EVENTS

Type of Event	Estimated Month/Year
Workshop	1
Exhibition	
Conference/ Symposium	1
Short Course	
Seminar	1
Other (please specify)	

10. DISSEMINATION TO PROFESSIONAL EVENTS AND SOCIETY

Type of Dissemination	Estimated Month/Year
Media	One by end of study
Public Presentation	
Other (please specify)	Will disseminate the knowledge gained by our research to the clinicians (ID Physicians/Medicine/Surgery/ Paediatrics/ICU by presenting our data in their morning meetings

SUMMARY OF BUDGET

SUMMARY OF BUDGET REQUESTED (OMR)*			
	Year 1	**Year 2**	**TOTAL**
Capital Equipment			
Recurrent Items (Consumables)	3400	2850	6250
Analysis & Data Processing Costs			
Use of University Facilities			
Conference Attendance			
Overseas Travel			
Local Travel and Transport Costs			
Insurance			
Research Assistants (B. Sc)			
Consultants			
Post-Doctorial			
Master's Scholarships			
PhD Scholarships			
Publication Costs		400	400
Miscellaneous		350	350
TOTAL	3400	3600	7000

* Refer to the budget caps

PERSONNEL TIME ALLOCATION		
	Year 1 (Hrs/Wk)	Year 2 (Hrs/Wk)
Principal Investigator	5	5
Co-principal investigator	4	4
Co-investigator	3	3
Technician		

Project Budget Breakdown (OMR)

CAPITAL EQUIPMENT	Year 1	Year 2	TOTAL
NA			
Subtotal			**Not applicable**

RECURRENT ITEMS (CONSUMABLES)	Year 1	Year 2	TOTAL
Antibiotics	2200	1900	4100
Genomic DNA extraction kits	750	650	1400
Tips, petri dishes and media	450	300	750
Subtotal	3,400	2,850	6,250

USE OF UNIVERSITY FACILITIES	Year 1	Year 2	TOTAL
Subtotal			0

CONFERENCE ATTENDANCE			
Destination	Year 1	Year 2	**TOTAL (RO)**
	Estimated Expenses	Estimated Expenses	
Within Oman			
Overseas			
Subtotal			Not Applicable

OVERSEAS TRAVEL			
Destination & Purpose of Visit	Year 1	Year 2	**TOTAL (RO)**
Subtotal			Not Applicable

LOCAL TRAVEL AND TRANSPORT COSTS			
Destination	Year 1	Year 2	**TOTAL (RO)**
Subtotal			-

INSURANCE	Year 1	Year 2	**TOTAL**
Subtotal			-

RESEARCH ASSISTANTS					
Number of RAs	Country	Present Position	Employment Period	Job Description	Expenses (RO)
Subtotal					**Not Applicable**

CONSULTANTS					
Full Name	Country	Present Position	Consultant Visit Period	Job Description	Expenses (RO)
NA					
Subtotal					-

Post-Doctorial				
Full Name	Country	Employment Period	Job Description	Expenses (RO)
NA				
Subtotal				-

MASTER'S SCHOLARSHIPS				
Number of scholarships	Country	Thesis Theme	Study Period	Expenses (RO)
NA				
Subtotal				-

PHD SCHOLARSHIPS				
Number of scholarships	Country	Thesis Theme	Study Period	Expenses (RO)
NA				
Subtotal				-

PUBLICATION COSTS	Year 1	Year 2	**TOTAL**
Q1/Q2 journal		400	400
Subtotal			400

MISCELLANEOUS	Year 1	Year 2	**TOTAL**
		350	
Subtotal		350	350
GRAND TOTAL			350

Collaboration:

1. Do you expect any collaborative arrangements to occur relating to the proposed Research Project?
2. If yes, please write the name and address of the collaborating organization/s:

Name of the Organization/Institution	**Address**
NA	NA

3. If you responded 'yes' to question 1, please detail the contribution provided by the collaborating organization/s

Particulars	Year 1	Year 2	**Total (RO)**
(i) Consumables			
(ii) Use of Facilities/Equipment			
(iii) Others (specify) Bioinformatics, Personnel, Travelling, Posters, Publications, Software			
(iv) Total Contributions			

الباحث الرئيس (جامعة السلطان قابوس)		
الاسم : ميهار ريزفي		
القسم: الأوبئة **والمناعة**	**الوظيفة:** أستاذ **مشارك**	**الهاتف:** ٩٩٥٢٧٧٤٨
الباحث الرئيس المشارك (جامعة السلطان قابوس)		
الاسم : زعيمة الجابري		
القسم: الأوبئة **والمناعة**	**الوظيفة:** أستاذ **مساعد**	**الهاتف:** ٢٤١٤
(الباحثون المشاركون – إن وجد)		
الاسم : زكريا المحرمي	**الاسم :**	
القسم : الأوبئة **والمناعة**	**القسم :**	
الاسم :	**الاسم :**	
القسم :	**القسم :**	
المدة الزمنية المقدرة للمشروع:		
المنحة المطلوبة (ر.ع)		
العام الأول:	**العام الثاني:**	**العام الثالث :**
عنوان مشروع البحث (تظهر فيه المتغيرات الأساسية)		
دراسة البكتيريا المسببة لاتهاب المسالك البولية: الجينات المقاومة لمضادات الميكروبات وفعالية الامضادات الحديثة لعلاج الاتهاب.		
ملخص مشروع البحث		
تساهم البكتيريا المقاومة لمضادات الميكروبات بشكل كبير في معدلات الاعتلال والوفيات لدى المرضى وارتفاع تكاليف الرعاية الصحية. OXA-48 هو النمط الجيني السائد المنتشر في عمان. تسبب ظهور الكاربابينيماتز ومقاومة الكوليستين في البكتيريا مشكلة بين المجتمعات العلمية والطبية والصحية العامة. تعد التهابات المسالك البولية واحدة من الأمراض البكتيرية الرئيسية في جميع أنحاء العالم ، ومع تصاعد مقاومة مضادات الميكروبات ، تزداد صعوبة علاجها.		

عادة ما يكون العلاج المفضل في مثل هذه الكائنات شديدة المقاومة هو كوليستين. لهذا يوجب اختبار مضادات الميكروبات التي تم إدخالها مؤخرًا في عمان ضدها في هذه الدراسة ، سنقوم بتقييم المظهر السريري وعوامل مضادات الميكروبات والفوعة ، وتقييم فعالية تركيبات مختلفة من الكولستين في المختبر والكاربابينيم مع العوامل الجديدة المضادة للميكروبات. بالإضافة إلى ذلك ، سوف نلقي الضوء على المحددات البكتيرية التي تمكن مضادات الميكروبات من تحقيق التآزر.

Declaration		
Principal Investigator Approval		
The principal investigator declares that he/she has prepared this proposal and that the ideas contained in it are original and that all provided information is accurate and correct.		
Name:	Signature	Date
Head of Department/ Director of Center Approval		
Name:	Signature	Date
DVCPSR/ Dean Approval		
Name:	Signature	Date