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RESEARCH ARTICLE

IMPACT OF ANTIMICROBIAL STEWARDSHIP PROGRAMMES ONBACTERIAL RESISTANCE LEVEL IN THE UAE: A SYSTEMATICREVIEW

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Abstract

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Antimicrobial resistance is a global problem that needs to be addressed immediately due to its huge clinical and economic burden ((WHO, 2021a). The death toll associated with antimicrobial resistance approached 5 million cases in 2019 while total cost that can impact the whole society is around £10 billion each year (Antimicrobial Resistance Collaborators, 2022: Smith and Coast, 2012). Eventually, this has motivated the World Health Organization (WHO) to set a global action plan to counteract the antimicrobial resistance all-over the world as a priority issue (WHO, 2015). In 2015, the United Nations (UN) released the updated Sustainability Development Goals (SDG) that is aiming to improve the public health and general well-being of the globe through tackling 17 topics. Treatment and prevention for multiple common infections such as Human Immunodeficiency Virus (HIV), malaria, tuberculosis and others were among the main targets in its agenda (UN, 2019). In UAE, although several initiatives have been adopted such as launching antimicrobial stewardship programmes and surveillance programmes, antimicrobial resistance is still an unresolved issue (National sub-committee for AMR surveillance, 2021; UAE Higher Committee for Antimicrobial Resistance, 2019). The resistance of Acinetobacter species to several cephalosporins and penicillins exceeded 20% (National sub-committee for AMR surveillance, 2021). Current evidence available publicly does not include a systematic review that is evaluating the effect of antimicrobial stewardship programmes on bacterial resistance level in UAE. With the scarcity of data and complexity of the issue, it is important to conduct this systematic review to assess the impact of these programmes on bacterial resistance level and identify gaps and challenges in the implementation.

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Introduction:-

Antibiotics

Antibiotics are part of the antimicrobial drugs (WHO, 2021a). They are agents used to treat or prevent infections caused by bacteria. Antibiotics either kill the bacteria (termed as bactericidal) or inhibit its growth (bacteriostatic) (Calhoun et al., 2021). Antibiotics are classified according to their chemical structures into several classes (Vazquez-Pertejo, 2020). They had a central role in fighting serious bacterial infections (such as sepsis) and saving lives through decades (CDC, 2021b; WHO, 2021a).

Nevertheless, it was revealed that almost one third of the antibiotics prescribed in the United States were not necessary or inappropriately prescribed. Accordingly, instead of obtaining benefits of the medication with no or limited adverse events, patients may suffer unnecessarily from avoidable safety and tolerability issues. Additionally, overuse and misuse of antibiotics has led to increase in bacterial resistance and inefficacy of several antibiotics that are currently available in use (CDC, 2021b; WHO, 2021a).

The development of new antibiotics is slowing down currently as it became less profitable business for pharmaceutical companies compared to medications for non- communicable diseases (Bushy et al, 2020; Cole, 2014). Additionally, restrictive measures from regulatory authorities are discouraging pharmaceutical companies to invest in new antibiotics (Abduelkarem et al, 2019). This raises the importance of vaccines, hygiene and infection control procedures as substitutes to prevent infections at the first place and reduce the reliance on antimicrobials (Bushy et al,2020). Vitamins and minerals such as vitamins C, D and zinc can strengthen the immunity and reduce the risk of infections as well (Maggini et al., 2017).

Antibiotic Resistance

Antimicrobial resistance is a defensive action where microorganisms fight drugs and abolish their effects through different mechanisms (Reygaert, 2018). Antimicrobial Resistance is a historical problem since ages. It is an anticipated consequence to the interconnection between different environmental elements (Munita and Arias, 2016; Reygaert, 2018).

The microorganism does not require developing resistance against each antimicrobial individually. Gene transfer between species and similarity between different antimicrobial agents allow for antimicrobial resistance to spread easily which add to the complexity of the issue (Munita and Arias, 2016; Reygaert, 2018). Additionally, transfer of resistance from animals to human through either food or faecal contamination has added to the burden of the problem (Reygaert, 2018).Moreover, the increase in number of immunocompromised people in society made the mission easier for the resistant pathogens to spread widely across the globe (Prestinaci and Pezzotti, 2015).As it is increasing remarkably, antimicrobial resistance became a global concern (WHO, 2021a). Around 1.27 million cases of death were directly related to antimicrobial resistance across 204 different countries throughout 2019. Out of all these cases, almost 79% were attributed to 3 main infectious diseases namely lower respiratory tract, blood stream and intra-abdominal infections (Antimicrobial Resistance Collaborators, 2022).

Likewise, only 6 bacterial pathogens were responsible for 927,000 deaths due to resistance issue. The most prevalent pathogens that were related to death cases due to resistance include E coli, Staphylococcus aureus, Acinetobacter baumannii, S pneumoniae, K pneumoniae and Pseudomonas aeruginosa (Antimicrobial Resistance Collaborators, 2022). Several factors contribute to this issue including inappropriate use of antimicrobials in humans, misuse to stimulate growth of animals, absence of guidelines for proper prescribing practice in hospitals (Aly &Balkhy, 2012; Landers et al., 2012). In addition to the scarcity of new antibiotics, resistance against current options will have a considerable burden on public health (Aly &Balkhy, 2012). In addition to increasing mortality and morbidity rate, this issue has a significant economic impact on society (Antimicrobial Resistance Collaborators, 2022).

Globally, it has been estimated that DALYs (Disability Adjusted Life Years) that are directly related to antimicrobial resistance is more than 47 million on average. While the death cases that are associated with the resistance are approaching 5 million cases (Antimicrobial Resistance Collaborators, 2022). Although the economic burden of the antimicrobial resistance appears to be low compared to other chronic diseases, but the economic model used for the calculation is not capturing all the required elements. It is estimated that it may costs less than £5 up to£20,000/patient/episode while it costs the whole society up to £10 billion/year (Smith and Coast, 2012).By 2050, this cost is expected to increase to reach up to $1 trillion per year (Dadgostar, 2019). Lengthy hospital stay, drug cost, isolation cost, surgeries cancellation, loss of productivity and death are all among the factors explaining the economic burden of the antimicrobial resistance (Dadgostar, 2019).

Antimicrobial resistance is a public health concern that can affect multiple segments in society (CDC, 2021a). The importance of addressing the issue of antimicrobial resistance has become more prominent because of the consequences associated with it. In 2019, almost 5 million deaths were associated to bacterial resistance alone without considering other types of microorganisms (Antimicrobial Resistance Collaborators, 2022). In addition to mortality, antimicrobial resistance may lead to other health comorbidities, extended hospital stays and consequently inflating healthcare cost (Antimicrobial Resistance Collaborators, 2022). Inefficacy of first line options and reliance on alternatives may lead to increase in the tolerability issues and safety concerns with patients (CDC, 2021a).

Persistence of the antimicrobial resistance will leave the healthcare system with no resources to fight critical infections in future (CDC, 2021a). The emergence of extensively-drug resistant pathogens (XDR) such as Salmonella typhi in Asia revealed that the healthcare system has already started to face this challenge (Akram et al., 2020). Furthermore, a drug such as Colistin (the last resort to fight the most resistant pathogens) has been reported to be ineffective (WHO, 2021a). This led the World Health Organization to consider antimicrobial resistance as a global threat due to its central role in the main infections that exist in the organization's agenda (Reygaert, 2018).

AntimicrobialStewardshipProgrammes

Antimicrobial stewardship programmes are plans to optimize the utilization of antimicrobials by implementing group of actions that are substantiated through scientific evidence (WHO, 2019). In addition to infection prevention/control and patient safety, antimicrobial stewardship is a core element in improving healthcaresystems. The holistic concept for antimicrobial stewardship is also applicable to sectors other than healthcare like agriculture and veterinary sectors (WHO, 2019).

Similarly to what is occurring in healthcare systems, antimicrobial resistance can develop due to overuse or misuse of antibiotics in agriculture or animal breeding (Majumder et al., 2020). Antibiotics are overly used in animal sector not only to treat infections but to enhance the growth as well (Landers et al., 2012). Accordingly, a holistic approach involving stakeholders from all segments (including agriculture and animal) is pivotal in combating antimicrobial resistance (Majumder et al., 2020). This is matching with the "One Health" approach that is supported by the WHO which is engaging different stakeholders and organizations to protect and reduce the risk for the global environment and eco-system (WHO, 2017). The antimicrobial stewardship approach is multidimensional, complex and requires collaboration between different stakeholders (CDC, 2021b; WHO, 2019).

International bodies such as the World Health Organization (WHO) and Centers of Disease Control and Prevention (CDC) have issued guidance for antimicrobial stewardship that can be implemented worldwide (CDC, 2021b; WHO, 2019).However, due to differences in needs and resources, each region/country can develop their own plans and initiatives (WHO, 2019).Furthermore, Antimicrobial stewardship programmes have specific objectives and aims. Their objectives typically include increasing education on the topic, research, infection prevention/control, justified use of antimicrobials and investing in new medical solutions (new antibiotics, vaccines and diagnostic tools). On the other hand, its aims are focusing on optimizing clinical practice related to antibioticprescription, enhancing patient outcomes, reducing microbial resistance, managing cost and boosting healthcare quality (WHO, 2019).

Surveillance programmes are part of the antimicrobial stewardship programmes that help to track and monitor resistance patterns and newly emerging trends in infection. Additionally, surveillance programmes are tool to spot the threats as early as possible and evaluate the impact of initiatives implemented (National sub-committee for AMR surveillance, 2021). However, there can be a bias of reporting only healthcare-associated infections on the expense of community-acquired infections (Perez and Villegas, 2015).

Culture-based detection for pathogens is a time-consuming process. Accordingly, this poses a challenge for antimicrobial stewardship programmes (McLain et al, 2016). Furthermore, several strains of bacteria as Atypical bacteria, are difficult to be isolated for detection (Stamm & Stankewicz, 2021). Factors like this may add to the complexity of dealing with antimicrobial resistance issue.Execution of antimicrobial stewardship programmes is challenged by several barriers and obstacles. Poor infrastructure, suboptimal laboratories, shortage of staff, lack of regulations and financial support are all among the elements holding back the proper implementation of antimicrobial stewardship programmes (ISID, 2022). Moreover, absence of leadership support and sponsorship put the programmesat risk of failure (ISID, 2022).From a different perspective, the unwillingness of healthcare professionals to adapt their practice is a major concern that need to be addressed wisely. Furthermore, antibiotics supply issue and lack of trust in laboratory results have been mentionedas strong reasons behind refraining from implementing the stewardship programmes (Rolfe et al, 2021).

OverviewonUnitedArabEmirates(UAE)

The United Arab Emirates is an Arabian country located in the southeast part of the Arabian Peninsula. As part of the Gulf Cooperation Council (GCC) region, UAE has common borders with both Saudi Arabia and Oman (Australian government department of foreign affairs and trade, 2022). It constitutes of seven emirates which are Abu Dhabi (the capital), Dubai, Sharjah, Ajman, Umm Al-Quwain, Ras Al Khaimah and Fujairah. More than 10 million are residing in UAE with almost 85% of the population are residing in 3 emirates only (Abu Dhabi, Dubai and Sharjah) (Australian government department of foreign affairs and trade, 2022; CIA, 2022).

Emirati nationals represent less than 12% from the general population while the remaining are expatriates from differentcountries and continents (Encyclopedia Britannica, 2022). People from different cultures and backgrounds respond differently to antibiotics prescription and use (Mangione-Smith et al., 2004). In regard to place of residence, almost 86.5% of the population are living in urbanized areas whilethe rest are inhabitants in rural places. However, there is inequality in healthcare services between urbanized and rural areas (Hannawi and Al Salmi, 2014).

Almost 5% of the UAE population are elderly people while the majority are in the age between 30-44 years which is the productive age (Encyclopedia Britannica, 2022).Generally, the immunity of elderly population is suboptimal which increase theincidence of infections (Chandra, 1992). Subsequently, the low percentage of elderly people may represent one of the factors that can help to decline infection rate in society. On the other hand, literacy rate is very high in UAE reaching up to almost 98% (CIA, 2022). High literacy rate may encourage the patients to participate in the decision related to their disease management. Additionally, they can have higher adherence levels to medical instructions and less probability of medical errors (Remshardt, 2011).

Expatriates in UAE represent diverse cultures and backgrounds coming from more than 200 countries across the globe. Long life expectancy of 78 years and strong economy of GDP exceeding 1.5 billion dirhams reflect the high standard of living and quality of healthcare in UAE (The official portal of the UAE government, 2022).Although the UAE economy relies heavily on income from petroleum sector, the government started to diversify the economy since 1990. It started to direct the focus to manufacturing, trade and tourism industries (Encyclopedia Britannica, 2022).

Figure1:- UAEMap. Source: vecteezy.com.

Figure1:- UAEMAP.

AntimicrobialResistanceinUAE

In UAE, although tremendous efforts have been made to contain the issue, antimicrobial resistance remains a major concern in country (Al Kaabi et al, 2011). Several pathogens have shown significant reduction in sensitivity to different antibiotics (Al Kaabi et al, 2011). Bacteria as Escherichia Coli showed high resistance against selected members in cephalosporin and penicillin class reaching up to 62%. Sensitivity of Klebsiella pneumonia to several antibiotics has diminished remarkably to reach as low as 55% against cefuroxime (National sub-committee for AMR surveillance, 2021). Moreover, Imipenem efficacy against Acinetobacter has severely reduced by almost 67% in 4 years period (Al Kaabi et al, 2011; UAE Higher Committee for Antimicrobial Resistance, 2019).

Conclusively, there was a rise in bacterial resistance across UAE in the period between 2010 and 2019 (National sub-committee for AMR surveillance, 2021). The government exerted huge efforts to curb this issue especially by realising new legislation of restricting antibiotic purchase without prescription. However, the self- medication rate is still rising and alarming for antibiotic misuse (Abduelkarem et al, 2019).

In order to overcome the antimicrobial resistance issue, different initiatives such as surveillance programmes, infection control plans and partnership with other sectors have been implemented (UAE Higher Committee for Antimicrobial Resistance, 2019). The Antimicrobial resistance surveillance programme started in UAE (Abu Dhabi) in 2010 then has been expanded to the rest of emirates in 2015. It is now part of the GLASS initiative (Global Antimicrobial resistance Surveillance System) that is initiated by WHO (National sub-committee for AMR surveillance, 2021).

GLASS is the first global initiative aiming to track antimicrobial resistance and detect the emergence of new trends early. It has a systematic process of data gathering, analysis and interpretation. It relies not only on laboratory results, but also on epidemiological research and clinical data (WHO, N.D.). In addition, GLASS initiative is monitoring the antimicrobial resistance in the whole environment including animals as part of the "One Health" approach (WHO, 2021b; WHO, N.D.).

However, still there is a gap present between the desired outcome and the actual one. The process of antimicrobial stewardship in UAE needs to be institutionalised rather than being person driven. Moreover, the scope of the programme must be expanded to cover the whole country instead of selected emirates. Finally, financialsupport needs to be considered independently for this aim (UAE Higher Committee for Antimicrobial Resistance, 2019).

RationalefortheResearch

Current literature available is discussing the implementation plan for antimicrobial stewardship programmes and resistance patterns for separate variable pathogens in UAE. Nevertheless, there is no recent comprehensive view on the progress occurred in reducing resistance because of the antimicrobial stewardship efforts.Subsequently, it is very important to conduct a research that compile the conclusion derived from previous literature and develop a systematic review to assess level of bacterial resistance in UAE.

ResearchQuestion

Based on the aforementioned data, the research question to be answered is "how effective were the antimicrobial stewardship programmes in UAE in order to reduce the bacterial resistance level against the most commonly prescribed antibiotics in the last 15 years?"

ResearchObjectives

The main objectives for this project were:

1. Assess the impact of antimicrobial stewardship programmes on bacterial resistance level in UAE.
2. Identify the gaps and challenges in designing and implementing antimicrobial stewardship programmes in UAE hospitals for future projects and research.

Methodology:-

To answer the research question, a systematic review process has been selected. The systematic review process allows to evaluate critically the existing evidence on the topic (Saks & Allsop, 2019). Additionally, it is considered as the highest level of evidence (Petrisor et al., 2006). Systematic review is a process where researcher locates articles on the selected topic from all possible references in an organized manner and synthesizes the evidence in a structured approach (Saks & Allsop, 2019). The search process should be inclusive and transparent to minimize the risk of bias. Additionally, steps should be clearly mentioned and documented to allow for reproducibility (Saks & Allsop, 2019).

SearchStrategy

Scientific databases on public domain were searched for available literature on the topic by following a systematic process. Selected databases that were accessible have been considered (Google Scholar, Pubmed, Scopus and grey literature). These databases have been selected due to accessibility opportunity and relevant literature that exist. In addition to these main databases, the online library of University of Essex has been searched for any additional article that was not captured in the main databases to complement the evidence available. In addition, hand searching for reference lists in the located articles was conducted as well to have a comprehensive list of articles (Saks & Allsop, 2019). Moreover, local reports from government like National Surveillance report and governmental websites were included (National sub-committee for AMR surveillance, 2021).

Predefined keyword terms were used in the search process including their synonyms to ensure that all relevant articles with different terminologies were captured (Saks &Allsop, 2019). Boolean operators have been applied to search for synonyms or combined words (Saks &Allsop, 2019).

Search process has been conducted in the following manner (impact OR effect OR influence AND antimicrobial stewardship OR AMS OR infection control OR ASP AND programme OR plan OR initiative AND bacterial resistance OR resistance AND UAE OR United Arab Emirates OR Dubai OR Abu Dhabi OR Al Ain OR Sharjah OR Ras Al Khaimah OR Ajman OR Umm Al Quwain AND antimicrobial OR antibiotic AND resistance pattern OR resistance level AND surveillance OR monitoring OR inspection) (Saks & Allsop, 2019). Double quotation marks were used for the keywords that consist of more than 1 word (EBSCO connect, 2018).

A summary for the databases, key concepts and filters used are mentioned in table 1 below. Search results were filtered to include only articles in English language and those that are published between 2007 and 2022. Rationale for this period is explained explicitly in the next section below (4.2 inclusion and exclusion criteria).

Databases	Key Concepts	Search Terms	Filters
PubMed	Impact	Imapct OR effect OR influence	Language: English
Scopus	Anitmicrobial Stewardship	Anitmicrobial Stewardship OR MAS OR Infection Control OR ASP	Date: 2007-2022
	Programme	Programme OR plan OR initiative	
Google Scholar	Bacterial resistance	Bacterial Resistance OR Resistance	Stage: Final
Grey Literature **Online Library for University of Essex**	UAE	UAE OR United Arab EmiratesOR Dubai OR Abu Dhabi OR AlAinORSharjah ORRasAlKhaimahOrAjman OrUmm Al Quwain OR Fujairah	Document type: scholarly journals (for Google Scholar only)
	Antimicrobial	AntimicrobialORAntibiotic	
	Resistance Pattern	Resistance Pattern OR Resistance Level	
	Surveillance	SurveillanceORMonitoringORInspection	

Table1:-Listofkeywordsandsearchtermsusedinthesearchprocess.

InclusionandExclusionCriteria

Antimicrobial resistance is a broad topic and dynamic as well. It addresses the resistance across different microbes in different time periods (Podolsky, 2018; Prestinaci et al., 2015). Accordingly, inclusion criteria helped to focus the search process and discussion areas on the desired topic only (Patino, C.M. and Ferreira, 2018). Inclusion criteria for this research include the following 1) Studies with any design that targeted assessing bacterial resistance of common pathogens in UAE; 2) Studies with any design that targeted antimicrobial stewardship assessment in UAE;3)Articles published in the last 15 years (2007-2022); 4) Studies in English language; 5) Studies that included any number of hospitals, medical centres or clinics in UAE; 6) Studies that are freely available.

The selection of the time interval for the publications is critical. The aim was to identify the resistance pattern throughout the time and the impact of the antimicrobial stewardship on it (including the surveillance system). The surveillance system was established partially in UAE (Abu Dhabi only) in 2010 then followed by the rest of the country in 2015 (National sub-committee for AMR surveillance, 2021). In order to obtain the resistance trend in chronological manner, articles on antimicrobial resistance published before implementation of surveillance system till 2022 were included. This will ensure that assessment for the resistance pattern will cover the pre and post periods for the implementation of the surveillance system. Eventually, tracking the change in resistance in chronological manner will be possible.

Accordingly, 15 years period for publications has been considered to cover this time interval.On the other hand, exclusion criteria ensure that articles that are out of scope of the research are not included (Meline, 2006). Exclusion criteria for this research included:
1) Studies covering viral or fungal resistance exclusively; 2) Incomplete studies or reports with preliminary results (abstracts or posters with sufficient data were included); 3) Non-English language studies; 4) Studies conducted on regional level without breakdown data; 5) Studies covering rare or uncommon bacteria only.

Screening
Manual screening has been conducted to all articles located in different databases. Screening process was conducted in 2 phases. Initial screening was conducted to filter the articles by titles and abstract. Second phase included filtering the articles through full text versions. Hand searching for reference lists of the located articles was applied to locate any relevant articles. Final selected articles were recorded in table with metadata on articles characteristics as shown below in table 3 in the data extraction sub-section (Eden et al., 2011; Littell et al., 2008). PRISMA diagram was used to describe screening and filtering process for the search results (Eden et al., 2011). PRISMA diagram is shown below at the results section (Figure 2).

DataManagement
Once database has been searched, search results list for Google scholar were saved manually. For Scopus, search results list was generated directly from the database. While for the online library for the University of Essex and the grey literature, manual list has been created. After screening, articles that met the inclusion criteria were downloaded and saved in a folder named (included). For articles that required a thorough reading to decide on inclusion, full text retrieved and saved in a folder named (further reading). The articles that were not meeting inclusion criteria but their reference list may include relevant papers were saved in the same folder named (further reading) for further hand search.

After hand searching the reference lists, selected articles were saved in a separate folder (hand search articles). Once all selected articles compiled in one folder, full text articles reviewed again for evaluation. At this final stage, if any article appeared to be out of scope or duplicate to a previously selected article it was saved in a separate folder named (excluded). All these folders were created manually and saved in the desktop of the used device.

CriticalAppraisal
Critical appraisal step for the final selected articles has been implemented using the JBI tool (Joanna Briggs Institute). Unlike CASP tool, JBI has the advantage of the presence of checklists that are not existing in the CASP (example: Checklist for prevalence study) (Brice, 2020; JBI, N.D.). Additionally, JBI tool provides clear and understandable questions that can be used easily by any researcher (Buccheri and Sharifi 2017). A separate appraisal sheet was used for each included study according to the study design with the results recorded in it. Relative strength of the study was determined by assigned score based on the answers (number of yes answers).The results sheets for all the studies appraised are attached in the appendix section. Different appraisal templates were used for different study designs. Templates for prevalence, quasi-experimental, case-control, systematic review, cross sectional and text/opinion studies have been used (Brice, 2020; JBI, N.D.).

Results:-

SearchResults
Collectively, 2344 articles and 2 reports (in PowerPoint format) have been located in all databases including Scopus, Google scholar, Pubmed, grey literature and theonline library for University of Essex. Scopus database has been searched using the keywords mentioned above for the period 2007-2022. Additionally, filter option has been applied and articles in English language and in final stage only have been refined and selected. Moreover, an article published in 2006 has been deselected. In total, the search results yielded 84 articles based on the keywords and filters applied. Review articles and systematic reviews were not excluded by filters. This was intended in order to check their data and reference lists manually to locate relevant articles if present.

The screening of 84 articles that were found in Scopus database revealed that none of them was matching the inclusion criteria. Articles were excluded because of the irrelevance to the topic, not covering bacterial resistance, being review articles/systematic reviews, not covering the UAE or regional studies without breakdown data. Hand searching for the reference lists of the located articles yielded one study (Moubareck et al., 2019) that was included in the review process.

Searching Google scholar database resulted in 2520 articles. After restricting publication period between 2007 and 2022, search results reduced to 2240 articles. English was selected as a default language in Google settings for search process. The search process included all types of articles that were screened and filtered at a later stage. Parentheses have been applied to the search terms to inform the search engine on the sequence of Boolean terms (McGill library, 2022).

Although the search process in Google Scholar yielded more than two thousand articles located, the search results can only show the first 1000 article (Harzing, 2010). Accordingly, the search process has been divided into 3 parts using 3 search periods (2007 to 2013, 2014 to 2018 and 2019 to 2022). The first search periodresulted 959, the second 703 and the third 494. In total, 2156 articles were located after the 3 search processes conducted. Comparing the search results when conducted on the whole period with that conducted on 3 consecutive periods revealed a discrepancy in total number of articles located.

Filtration of the 2156 articles located on Google scholar has ended to 4 articles that were included directly and 7 articles that were located after hand search for the reference list in primarily located articles. Different 7 articles have been excluded although they were matching inclusion criteria in the initial screening phase.

Exclusion reasons were 1) date range for data collection is out of scope (before 2007); 2) not accessible; 3) abstract version with limited data. In total, 11 articles have been included in the process from the Google scholar search.In addition to the classical scientific databases, grey literature has been searched as well to avoid publication bias and ensure inclusiveness and balanced view (Paez, 2017). BASE (Bielefeld Academic Search Engine) has been used to check the unpopular articles. However, no relevant articles have been found on the database. Similarly, ProQuest has been searched for relevant dissertations and theses using the same criteria and filters. In total, 18 dissertation papers have been located on the database. Validation of the 18 dissertations located on ProQuest revealed that no article has met the inclusion criteria.

In parallel, websites for UAE government and WHO have been checked for official reports. A surveillance report for antimicrobial resistance in UAE was located on the official portal for the ministry of health (National sub-committee for AMR surveillance, 2021). Additionally, 2 reports in the form of power-point presentation format were found on the official website for the international conference on antimicrobialresistance (ICAMR) (Abdulrazzaq, N.D.; Thomsen, 2019). Lastly, one conference abstract has been located on the ESCMID conference website (Thomsen and Abdulrazzaq, 2019). In summary, Grey literature search resulted into 1 report in article format, 2 reports in power-point format and 1 conference abstract. All of the located materials were included in the review process.

In addition to the main databases, the online library for the University of Essex has been surfed to locate relevant articles. The use of the advanced search option allowed applying different filter types in order to have more focused search results. Boolean operator, scholarly journals and the search within the full text were permitted in the process. Moreover, related terms and articles available in library collection were allowed as well. The English was the only language selected in the search process. Lastly, Publication date has been restricted to include only the period between 2007 and 2022.

Searching the online library for the University of Essex has led to 84 articles on the topic. The number of articles has been reduced to 79 after removal of exact duplicates. After screening, no articles have been found as relevant. One article was found as relevant and met the inclusion criteria but excluded at the end as it covers date range which was out of scope. Another article has been excluded due to accessibility issue (not open access). The hand searching for the reference lists for located articles yielded 4 articles that were considered as relevant.
Searching Pubmed database using the same criteria and filter options has not revealed any article. Accordingly, the screening step has not been conducted for this database. In summary, 19 article/report from all databases that have met the inclusion criteria and were included in the review process after excluding 1 additionalarticle due to

duplication. Screening results for all databases and mode of locating articles have been mentioned in details in Table 2 below.

Article	Year of Publication	Database Searched	Method of Locating Article
Alqahtani et al.	2021	Google Scholar	Directly located from database
National Sub-Committee for AMR surveillance	2021	Grey Literature	Official portal for Ministry of Health- UAE
Sadeq et al.	2021	Google Scholar	Directly located from database
Moubareck et al.	2019	Scopus	Hand search for list of references for the located articles
El Lababidi et al.	2019	Google Scholar	Directly located from database
Thomsen	2019	Grey Literature	website for the international conference on antimicrobial resistance
Thomsen & Abdulrazzaq	2019	Grey Literature	ESCMID conference website
Al Hosani (dissertation)	2018	Google Scholar	Directly located from database
Moubareck et al.	2018	Google Scholar	Hand search for list of references for the located articles
Sonnevend et al.	2016	Online Library for University of Essex	Hand search for list of references for the located articles
Sonnevend et al.	2015	Online Library for University of Essex	Hand search for list of references for the located articles
Zowawi et al.	2015	Online Library for University of Essex	Hand search for list of references for the located articles
WHO	2014	Google Scholar	Hand search for list of references for the located articles
Sonnevend et al.	2013	Google Scholar	Hand search for list of references for the located articles
Dash et al.	2013	Google Scholar	Hand search for list of references for the located articles
Alfaresi et al.	2011	Google Scholar	Hand search for list of references for the located articles
AlKaabi et al.	2011	Google Scholar	Hand search for list of references for the located articles
Weber et al.	2010	Google Scholar	Hand search for list of references for the located articles
Abdulrazzaq	N.D	Grey Literature	website for the international conference on antimicrobial

			resistance

Table2:- Screeningresultsforalldatabasesandmodeoflocatingarticles.

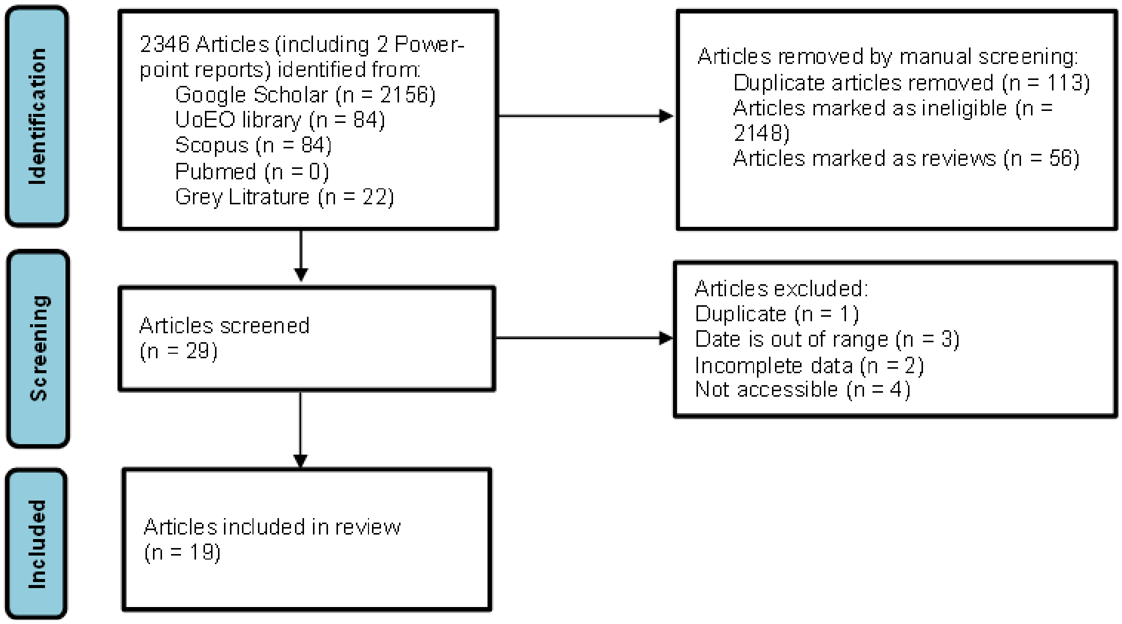

Figure2:- PRISMAdiagramandscreeningresults.

CriticalAppraisalResults

All the final 19 selected articles have been critically appraised using the JBI tool. The first paper appraised was for poster that was presented at ECCMID conference in Vienna in 2010. Checklist for prevalence study was used for assessment as the study design was similar to that type of research. Although that random sampling for isolates was followed but details on the sampling type was not mentioned.

Additionally, the sample has been obtained from1 hospital only. Overall, the paper quality was acceptable as the pathogen isolation and testing process was mentioned in detail. Similarly, data analysis and results were presented clearly along with conclusion section that fulfilled the research objectives (Weber et al., 2010).

Assessing Alfaresi et al, (2011) study using prevalence study checklist revealed a moderate strength for the quality of the study except for missing to mention sampling technique. On the other hand, the study involved 3 different hospitals allowing for generalizability of the results. Additionally, isolates identification and data analysis have been mentioned clearly. Finally, although sample size was relatively large, but it was not mentioned on which basis it was selected. (Alfaresi et al., 2011).

Another study was comparing the emergence of resistance against antibiotics and compared with the results of a previous study. Although the hospital settings and procedures were the same in both studies, variability occurred through different workers and data on antibiotic/strain. Moreover, tracking sensitivity trend only occurred in the recent study exclusively. On the other hand, confounding factors or any actions for mitigating them were not mentioned clearly. Finally, the process of selecting the isolates was not mentioned clearly for comparison between the 2 groups/studies (AlKaabi et al., 2011).

Assessment of the epidemiology of Acinetobacter baumannii in Abu Dhabi was conducted in 2013. The study sample was collected from 5 different hospitals in Abu Dhabi which may reflect the generalizability of the outcomes. Sampling approach details were not sufficient, but it was close to the cluster sampling by collecting all relevant isolates from the hospitals. There was insufficient data on sample size calculation. The response rate from participating hospitals was not equal as isolatesfrom Al Rahba hospital was low. On the other hand, sample testing/analysis and data analysis process were structured in the paper (Sonnevend et al., 2013).

One of the included studies in the review process was Dash et al (2013) study that focused on the emerging resistant strain of Klebsiella Pneumonia – NDM (New Delhi Metallo Beta-lactamase). The samples collected were consecutive and clinically relevant. The selection process details were not clear. Moreover, No evidence has been mentioned on the validity of sample size. In contrast, the sample identification and analysis process were detailed explicitly. Furthermore, Data analysis covered all the samples involved (Dash et al., 2013).

In 2014, WHO released a report for surveillance on antimicrobial resistance. The report relied on systematic approach to critically appraise the included studies before data synthesis. Accordingly, checklist for systematic review was used for evaluation. The objective and inclusion criteria were clearly stated. The included studies in the report were assessed using GRADE method but were not clear how many experts conducted the review process. The risk assessment plan was considered as well.

Finally, the gaps and future actions were recommended to improve surveillance and reduce resistance (WHO, 2014). Sonnevend et al (2015) study demonstrated an acceptable quality with enough details mentioned on sample testing procedures and data analysis. Moreover, isolates were collected from 8 different hospitals in UAE. However, 82% of the samples were collected from only 3 hospitals with low response rate from the other 5 hospitals. On the other hand, sampling technique and sample size calculation were not sufficiently detailed (Sonnevend et al., 2015). Prevalence study checklist was used to appraise the quality of this paper.

Another study conducted to identify the epidemiology of Acinetobacter Baumanii that is carbapenem resistant in the Gulf countries including UAE (Zowawi et al., 2015).From UAE, 8 isolates were collected from 1 hospital only which may affect external validity and pose questions on response rate for the participating hospital. Although sampling technique and calculations were note detailed, sample size generally appears low and may not be representative. Inclusion criteria for the isolates were stated in details in addition to the sample analysis and data analysis procedures. As this was an epidemiological study, prevalence study checklist has been used for assessment (Zowawi et al., 2015).During the critical appraisal phase, one of the included studies was missing critical data such as the exact date of the isolates collection and the breakdown number of isolates for UAE (as the study was a regional one) (Sonnevend et al., 2016).Accordingly, the study has been excluded from the review process.

One of the included studies was a dissertation for Doctor of Public Health degree on epidemiology of tuberculosis in Abu Dhabi. The study showed a great level of acceptability regarding the sampling approach and data analysis. All the records in the databases used were included in the analysis process. Accordingly, there was no need to rely on sample size calculation. Data collection and analysis details were stated in a clear manner (Al Hosani& Ismail, 2018). Prevalence checklist has been used for the evaluation of this paper.

Moubareck et al. (2018) study demonstrated modest quality by using prevalence checklist template. Sampling process was not stated clearly and sample size validation was not documented. Moreover, no selection criteria were used when submitting the isolates to the laboratory. Furthermore, contribution of eachparticipating hospital regarding the number of isolates provided was not discussed. However, details on susceptibility testing, molecular typing and data analysis have been highlighted in the study text (Moubareck et al., 2018).

On a different note, Moubareck et al (2019) study showed a good level of elaboration on susceptibility and gene testing. Similarly, explicit data was shared regarding analysis process and resistance measurement. However, inclusion criteria were not clear in the methodology. Moreover, the study failed to consider the confounding factors or its mitigation plan (Moubareck et al., 2019). The assessment has been conducted by applying cross-sectional checklist.

El Lababidi et al (2019) study was assessed by using the quasi-experimental checklist. The implementation of the ASP preceded the study enrolment. This may help to establish causality between the exposure and outcome (Saks & Allsop, 2019). Comparison group was the same group of the study but parameters were measured at the baseline to compare with the outcomes after 2 years. Accordingly, outcomes were measured pre & post the exposure. Measurement tool & statistical analysis were explained explicitly. Although follow up period mentioned in the study, but the exact details related to this follow up period were missing (El Lababidi et al., 2019).

An expert opinion document has been located in a power-point format on the public domain as part of the grey literature. The role of the author was pivotal in the UAE higher committee for Antimicrobial Stewardship program.

The quality of evidence may be considered low as it is a presentation for expert opinion rather than structured research (Petrisor and Bhandari, 2007). However, the source of data mentioned were the national surveillance database and WHO reports. PRISMAdiagram and logical sequence have been mentioned in the document explaining the collection process and susceptibility testing. Additionally, breakdown data has been stated regarding resistance pattern of different pathogens against several antibiotics (Thomsen, 2019). Text and opinion checklist has been used for validation.

Another opinion paper was evaluated using the text and opinion checklist to validate the quality of evidence provided. This paper has been located on the website of ICAMR conference. Similarly, its data has been derived from either the national surveillance system or WHO reports. The data explored in the document is a result of logical sequence of actions related to pathogen isolation, testing and resistance tracking approach in the country. However, not all the data mentioned was substantiated with the proper reference. Final results and resistance patterns for several pathogens were matching with the data from the previous report (Abdulrazzaq, N.D.; Thomsen, 2019).

An abstract paper was located in the grey literature and evaluated by the prevalence checklist template. Although the paper was found as an abstract only with missing details on the collection and analysis process, but the outcomes data were mentioned with clear figures. Accordingly, it has been decided to include the paper in the review process. Samples were collected from the national surveillance system where the network comprises of 177 sites. The paper was lacking data about sampling technique and proper sample size. Moreover, the paper is an abstract; it didn't include enough details on the setting of the sample collection or data analysis (Thomsen & Abdulrazzaq, 2019).. However, GLASS protocol developed by WHO was followed which infer that the researchers followed a standardized procedure. Similarly, WHONET-2018 softwarehas been used for analysis which concluded that a structured analysis scheme has been adopted (Thomsen & Abdulrazzaq, 2019).

In 2021, a paper was published discussing the prevalence of CRG (Carbapenem Resistant Genes) among ICU (Intensive Care Unit) patients in hospitals of Gulf countries. According to appraisal utilizing prevalence checklist, the paper is lacking details on sample size calculation or sampling method. Furthermore, sampling frame was developed only for ICU patients in the participating hospitals. However, hospitals/patients characteristics, molecular detection technique, analysis method and breakdown results were mentioned in details (Alqahtani et al., 2021).

The National Sub-Committee for AMR Surveillance in UAE published a surveillance report in 2021. The report considered all the isolates in the system initially. Later, isolates were excluded after applying the inclusion criteria. Accordingly, sample size dimensions and sampling method were not needed. The data collection process, analysis and interpretation were mentioned clearly. Additionally, WHONET software has been used for analysis. However, response rate from participating hospitals was not discussed (National Sub-Committee for AMR Surveillance, 2021). The critical appraisal process has been practiced using prevalence study template.

The last paper selected was published in 2021. It discussed the influence of multi- disciplinary team (MDT) on improving the stewardship approach. The study was designed in a quasi-experimental manner. The groups were comparable except in some settings where the male population were more in non-intervention group compared to intervention group. Additionally, the study was comparing the influence of the stewardship by measuring the required outcomes before and after theintervention (MDT). Comparison was established between both groups in a clear manner to evaluate the effect of the intervention (Sadeq et al., 2021).The details on follow up period were missing in the study. However, the outcomes has been measured objectively and the analysis has been conducted using a standardized approach. Finally, different analytical approaches were applied to assess different measures targeted (antibiotic consumption, length of stay, microbiological outcomes. Etc) (Sadeq et al., 2021).

DataExtraction

The metadata for the final selected 19 articles were extracted and displayed in (Table 3) below. A score for each article assigned based on the number of "Yes" answers in the appraisal template.

	Author	Year ofpublica tion	StudyPeriod	Samplesize	Pathogen	BacterialResistance	Score
1	Alqahtan	2021	2019	529	*CRG*	16.8% of the	5/9

	i etal.			(allGCC countries)and 83fromUAE only	*(CarbapenemResistantGenes)*	specimenscontain 1 or more of theCRG in UAE (calculationhas been made to thebreakdowndata for countries)	
2	National Sub-Committee forAMR surveillance	2021	2019& 2010-2019	482,312 isolates	*All pathogens(then focusedanalysis on themost important 9bacteria)*	High carbapenemresistance from *A.baumanii&P.aeruginosa*(25%& 14.4%) and highCephalosporinresistance (ceftriaxone& cefotaxime) from *E.coli* &*K. pneumonia*(31.9%&32.5) and (24.7%&26.5%) respectively	8/9
3	Sadeq et al.	2021	2020-2021	3000 patients	*MDRO (MRSA,VRSA,VRE, ESBL, Acinetobacterandothers)*	Increase in cases of*Clostridium difficle.* Alsoreduction in *MRSA*-MDRO in interventiongroup.However, there was an increase in *ESBL*.Although,infection cure	8/9
4	Moubareck etal.	2019	2015-2016	37	*Pseudomonasaeruginosa withlow sensitivity tocarbapenem*	24% of the isolates werecarbapenem resistant.Therearediverse mechanisms ofresistanceamongthe pathogen	5/8
5	El Lababidi etal.	2019	2015-2017 then 2yearsfollowup	NA	*NA*	Rate of hospital-onset *C.difficile*&MDRinfections reduced dueto ASPin CCAD	8/9
6	Thomsen	2019	2010-2018	385,472	*Allpathogens*	High resistance fromgram negative and*Enterobacteriaceae*against third generationcephalosporins. Highresistance from*AcinetobacterBaumanii* against crabapenem.	4/6
7	Thomsen &Abdulrazzaq	2019	2017	NA	*Priority, High &Mediumimportancepathogens*	High resistance rateamong priority, high &medium importancepathogens mainly (*A.Baumanii*36%,*P.*	5/9

						*aeruginosa*20%)	
8	Al Hosani(dissertation)	2018	2012-2015	3350	*Tuberculosis*	No major change overtime. TB MDR ratedeclinedslightlyfrom 2012to2015	8/9
9	Moubareck etal.	2018	2015-2016	89 (from 5hospitals,private &public)	*CarbapenemResistantEnterobacteriaceae*	High rate of colistinresistant CRE. Alsoemergence of resistantstrain of *K. pneumonia*.Allstrainswere MDR and1thirdwereXDR	5/9
10	Sonnevend etal.	2016	NA	75(UAE notmentioned)	*Colistin resistantEnterobactriaceae*	Breakdown data is notclear so study wasexcluded.	NA
11	Sonnevendet al.	2015	2009-2013	200(56 fromUAE)	*Enterobacteriaceaestrains*	InUAE, all strains were MDR,66%XDR	6/9
12	Zowawi et al.	2015	2011-2013	117(8 fromUAE)	*Carbapenem-ResistantAcinetobacterbaumannii*	All UAE isolates have theOXA-23andOXA-51 genes responsible for *A.Baumanii*difficult typeofresistance.Also carbapenemco-resistance to other antibiotics (no specific data for UAE)	5/9
13	WHO	2014	2013	NA	*MultiplePathogens*	Variable but generallyhigh. Except for *K.pneumonia*resistanceto Carbapenems	7/11
14	Sonnevend etal.	2013	2008	110	*Acinetobacterbaumannii*	High level of resistancegenerally. Exceptcolistin, all ABs hadresistance. All epidemicstrainswereMDRand 60% wereXDR	6/9
15	Dashet al.	2013	2011-2012	202	*K.Pneumonia*	7% of *K. Pneumonia*isolates were CRKP.13/14ofthemhasNDM genes	7/9
16	Alfaresietal.	2011	2008	662	*ESBL (E.coli &K.Pneumonia)*	Emergence of ESBL-producing *E. Coli & K.Pneumonia*(inparticular (CTX-M-15gene)	5/9
17	AlKaabi etal.	2011	2004-2008	NA	*MRSA,P Aurigonosa, E.Coli, K.PneumoniaAcinetbacter*	*E.coli & k. Pnuomnia*appearedtobedominant and increasinggradually	6/10
18	Weberet al.	2010	2009	62	*MRSA*	Diversity of strains andhigh prevalence ofresistantPVL genes	6/9

						(42%)	
19	Abdulrazzaq	N.D	2010-2017	NA	*Allpathogens*	High resistance ratefrom priority pathogens(*A. Baumanii*, *P.aeruginosa* &*Enterobacteriaceae*and even*S.Pneumonia*	4/6

Table3:- Summaryfordataextractionforincludedarticles.

Discussion:-

The final studies selected were variable regarding pathogen tested. The range covered by the studies included single pathogens, multiple pathogens and entire family of pathogens. Moreover, the studies covered a long range of time from 2010 till 2021 (date of publication). variability of pathogens across this time range posed a37challenge in interpreting and synthesizing the data. Accordingly, it has been decided to apply a chronological approach in data interpretation and compile the studies that discuss the same pathogen/s. Thematic analysis was applied to draw conclusion by using 3 main concepts as follows 1) Resistance was increasing 2) Resistance was decreasing 3) No change in resistance (Saks & Allsop, 2019).

MRSA

The first pathogen that has been assessed was staphylococcus aureus in UAE against several antibiotics. According to Weber et al. study (2010), there was a considerable level of variation between strains of Methicillin-Resistant Staphylococcus Aureus (MSRA). Variability of strains was representing the diversity of host characteristics which was evident in UAE population diversity including both locals and expatriates (Weber et al., 2010). Additionally, PVL (one of the genes responsible for MRSA resistance) had high prevalence rate of 42% across the different strains of MRSA (Weber et al., 2010).AlKaabi et al (2011) study highlighted the decline in sensitivity of staphylococcus aureus to Oxacillin antibiotic compared to a study that was published earlier on the same topic from 94% down to 84.4%. The sensitivity decline of the pathogen was consistent across several years from 2002 till 2008. Furthermore, the rate of MRSA has increased from 5% to 15.6% compared to the previous study (AlKaabi et al., 2011).

Moving to 2014, the World Health Organization (WHO) issued a report on resistance surveillance across the globe which showed MRSA prevalence reached 27.5% in 2012 in UAE (WHO, 2014). Except for the trend showing decline in MDRO prevalence including MRSA, the surge in MRSA prevalence has been identified in 2017 as 36% (Abdulrazzaq, N.D; El Lababidi et al., 2019).

The prevalence of MRSA resumed to increase to reach 36.3% in 2018 (Thomsen, 2019). Resistance of both Methicillin-resistant Staphylococcus Aureus (MRSA) and Methicillin-Susceptible Staphylococcus Aureus (MSSA) was mainly against fluoroquinolones, erythromycin and sulfamethoxazole/trimethoprim. Abu Dhabi was the highest emirate in resistance rate of MRSA against oxacillin which was equal to 38.7% (Thomsen, 2019).

While in 2019, MRSA prevalence recorded slightly lower rate at 35.3% mainly against oxacillin. Like the data published by Thomsen in 2019, MRSA resistance was mainly against Fluoroquinolones, erythromycin and sulfamethoxazole/trimethoprim (Thomsen, 2019; National sub-committee for AMR surveillance, 2021). Even, prevalence of MRSA against beta-lactams reached up to 35% in 2019 (National sub- committee for AMR surveillance, 2021).

Finally, in 2021, the total number of cases for MRSA and MDRO (Multi-Drug Resistant Organism) decreased by more than 50%. Unfortunately, there was no split for the figures to show the contribution of the MRSA cases only. Moreover, the study conducted in 1 hospital only to show the impact of antimicrobial stewardship program on several outcomes. However, the supplementary material was showing decline in the MRSA infections per 100 adult patient days (from 8 to 5) (Sadeq et al., 2021).

In conclusion, observing the thematic analysis for the pathogen revealed that resistance was increasing consistently from 2008 till 2019 (except with decline in 2021 that was for the whole MDRO group without breakdown on MRSA).Additionally, MRSA prevalence was increasing steadily to reach the highest rate in 2019 followed by decline in MRSA infection rate in 2021 (AlKaabi et al., 2011;National sub-committee for AMR surveillance, 2021; Sadeq et al., 2021; Thomsen, 2019).

ESBL/Enterobacteriaceae

The second part of the discussion is on the resistance pattern for Enterobacteriaceae strains including ESBL pathogens mainly E.coli and K. Pneumonia. In 2011, Alfaresi et al. (2011) study published an interesting data about circulation of ESBL pathogens in 2008 carrying different resistance genes as CTX and SHV. For the ESBL-producing E. Coli, 94% of the sample were carrying the CTX gene. On the other hand, K. pneumonia that carried the CTX gene was equivalent to 64.4% and 32.2% were carrying SHV gene (Alfaresi et al., 2011). Based on this, the data reflected the increasing trend for resistant ESBL pathogens in 2008 (Alfaresi et al., 2011).

Additionally, in 2008, sensitivity of the E. coli to several antibiotics such as, ciprofloxacin, amikacin, and gentamicin has declined significantly compared to previous years (Alkaabi et al., 2011). Moreover, sensitivity to other beta-lactams as amoxicillin/clavulanate has declined significantly as well. On the other hand, sensitivity of K. Pneumonia against all examined antibiotics has not changed significantly over time. However, the prevalence of ESBL E. coli and K. Pneumonia has increased in the same period (Alkaabi et al., 2011).

One of the few studies in this review that was focusing on single pathogen is Dash et al. (2013). This trial studied the emergence of K. pneumonia strains that are resistant to carbapenem class. Samples under study were collected from September 2011 till October 2012. Prevalence of Carbapenem-Resistant K. Pneumonia (CRKP) reached 7% from the total samples collected. Almost 93% of the CRKP identified were carrying the NDM gene (New Delhi Metallo Beta-lactamase) (Dash et al., 2013). It isa new gene coding for enzyme that renders the K. Pneumonia resistant to beta- lactam antibiotics (Raghunath, 2010). Although the emergence of the NDM CRKP, the results were driven from a study conducted in 1 hospital only in UAE which put concern on generalizability (Dash et al., 2013).

Data collected in 2012 revealed that E.coli resistance in UAE reached up to 22% against cephalosporins (third generation) while against fluroquinolones was 33.3% (WHO, 2014). In the same period, resistance of K. pneumonia against third generation of cephalosporins and carbapenems was 17.4% and 1.5% respectively (WHO, 2014). On a similar note, a regional study conducted between 2009 and 2013 to assess the distribution of Carbapenem-Resistant Enterobacteriaceae (CRE) in the Arabian Peninsula and its characteristics. Although the small sample size collected from UAE, the results were showing predominance for the resistant strains of Enterobacteriaceae family pathogens. Only 19.6% of the sample collected from UAE did not have any gene for carbapenemase activity while the rest either have single gene or multiple genes (Sonnevend et al., 2015).

Additionally, 19.7% of the sample were carrying genes responsible for ribosome- modifying enzymes that can render the bacteria resistant to other antibiotics such as aminoglycosides (Ghotaslou et al., 2017; Sonnevend et al., 2015). K. Pneumonia represented 73% of the sample collected while E. Coli was 18% only. Moreover, XDR was estimated to be 66% while the resistance to antibiotic such as tigecycline was 28.6% (Sonnevend et al., 2015).Another regional trial was Sonnevend et al., (2016) that focused on Enterobacteriaceae resistance to colistin. However, the full breakdown for the results per country was not available. One of the breakdown data available was showingpresence of multiple resistance genes in E. coli strain isolated from UAE. In addition to colistin, this strain was resistant to other antibiotics such as carbapenems, cephalosporins, tetracyclines and fluroquinolones (Sonnevend et al., 2016).However, as the study did not meet inclusion criteria (no enough details on breakdown data in UAE) it was excluded from analysis.

Shifting to 2015-2016, Moubareck et al. (2018) study demonstrated the prevalence of CRE among Enterobacteriaceae isolates as 4.6%. K. pneumonia CRE isolates was around 16.2% from the total K. pneumonia sample. The total CRE sample was mainly comprising of K. Pneumonia (79%) and E. coli (15%) that all of them were MDR. The prevalence of XDR was 32.6% among all isolates mainly driven by K. pneumonia which was 40%. Surprisingly, 5.7% of the K. Pneumonia were Pan-Drug Resistant (PDR). On the contrary, tigecycline and colistin were effective against E. coli that has no XDR isolates. Finally, K. pneumonia ST14 group was found to be an XDR and harboring both NDM and OXA 48-like genes. Regarding CRKP, almost 31.4% were colistin resistant as well (Moubareck et al., 2018).

However, pattern showed decline in MDRO infections including Enterobacteriaceae from 2015 till 2017 (2.39 cases to 0.38 cases/1000 patient days) (El Lababidi et al., 2019). In 2018, resistance level of CRE estimated at 4.4% while ESBL at 34.4% and pipracillin/tazobactam was highly effective against the Enterobacteriaceae. On the contrary, third generation cephalosporins and cotrimoxazole were highly ineffective against Enterobacteriaceae and ciprofloxacin ineffective against E coli. It was documented that an outbreak for K. Pneumonia has set in UAE in

2011 resulted in 5 deaths for infants in neonatal ICU (NICU). Similar outbreak happened in Abu Dhabi in the same year for E. coli that was not either ESBL or CRE and no death cases were mentioned (Thomsen, 2019).

These figures were slightly different from 2017 data that showed CRE resistance at 4.8% and ESBL at 31.3% (Abdulrazzaq, N.D). Similar results have been published in 2019 (most probably using the same data) (Thomsen & Abdulrazzaq, 2019).Accordingly, this infers a slight reduction in CRE resistance and increase in ESBL cases.

Distribution of carbapenem resistance genes (CRG) in Gulf region has been assessed again in a study published in 2021. Two hospitals from UAE participated in this study (one for adult cases while the second for children's cases). Prevalence of CRG was 20.8% among adults and 11.4% for paediatric group in 2019. However, the sample size was relatively small, and the samples were collected from ICU patients only which pose risk on external validity concept. The study highlighted important facts and interpretations from the results as well. First, probability of CRG infections increases with age and length of hospital stay. Second, possibility of CRG was high when the patient was on antibiotic treatment during hospital admission compared to those not on antibiotics (Alqahtani et al., 2021).

National Sub-Committee for AMR surveillance in UAE released a report in 2021 on the resistance pattern across the country (based on 2019 data). The report showed relatively low resistance prevalence from Enterobacteriaceae and K. Pneumonia against carbapenems equal to 4.3% and 4.5% respectively. Nevertheless, these resistance percentages increased remarkably for ESBL strains to reach 27.6%, 32.5% and 26.5% for Enterobacteriaceae, E. Coli and K. Pneumonia respectively. The resistance for K. Pneumonia ranged from 3.4% against aminoglycosides to 29% for ESBL while sensitivity to fluoroquinolones was as low as 58%. Similarly, the resistance for E. coli ranged from 0.3% for aminoglycosides to 62% for aminopenicillins (National Sub-Committee for AMR surveillance, 2021).

Sensitivity of the E. coli to fluoroquinolones was as low as 59%. Even further, prevalence of MDR has increased for both E. coli and K. pneumonia from 2010 to 2019 to reach 45% and 35% respectively. Increasing resistance trend for both E. coli and K. pneumonia was evident against several antibiotic classes such as beta- lactams, carbapenems and fluoroquinolones (National Sub-Committee for AMR surveillance, 2021).

Application of Antimicrobial Stewardship Program did not reduce the prevalence of ESBL infections that increased as per Sadeq et al. (2021). The increase was attributed to improper use of antibiotics unnecessarily. In contrast, total MDRO was showing reduction in the intervention cohort. However, the study did not mention the breakdown figures for the different strains in the MDRO group and their contributions (Sadeq et al., 2021).

In summary, resistance pattern for Enterobacteriaceae was fluctuating during the period covered by the research. While in the beginning it showed high prevalence for ESBL, K. pneumonia did not show any significant change (Alkaabi et al., 2011).Later, ESBL strains for E. coli and K. pneumonia started to increase and resistance against several antibiotic classes erupted rapidly from 2012 till 2019. Moreover, increase in MDR and emergence of PDR strains have been documented in this period (Dash et al., 2013; Sonnevend et al., 2015; WHO, 2014; National Sub-Committee for AMR surveillance, 2021). Overall. Resistance of Enterobacteriaceae (Especially ESBL strains) was increasing throughout the whole period.

Acinetobacter

Acinetobacter species sensitivity to several antibiotics such as carbapenems, cephalosporins, fluoroquinolones and beta-lactams declined significantly from 2004 till 2008. Susceptibility to antibiotics such as imipenem declined to 32.5% and piperacillin/tazobactam to 29.6%. Similar trend has been observed against cephalosporin agents. The Emerging resistance from this pathogen reduced the options available to combat the organism (AlKaabi et al., 2011).

Acinetobacter baumannii has become one of the highly important pathogens globally due to its resistance level and multiple variants developed (Sonnevend et al., 2013). In 2008, Except for colistin, Acinetobacter baumannii showed high resistance level to all antibiotics tested including carbapenems, ciprofloxacin and piperacillin/tazobactam. Most of the strains were epidemic (72.2%) while the remaining were sporadic. All epidemic strains were labelled as MDR and 60% of them as XDR (Sonnevend et al., 2013).

A regional study assessed the epidemiology of Carbapenem Resistant Acinetobacter baumannii (CRAB) revealed that all isolated strains were carrying OXA-23 and OXA- 51 genes that are responsible for the pathogen resistance. Additionally, prevalence of carbapenem co-resistant strains was high for the entire sample (no specific data for

UAE). However, the results of UAE derived from small sample (8 isolates) received from one hospital. Apparently, this will hinder the generalizability of the results to the rest of the country (Zowawi et al., 2015). However, El Lababidi et al. (2019) study showed decline in MDRO infections (including Acinetobacter baumannii) but without breakdown data to understand the pathogen contribution (El Lababidi et al., 2019).Compared to the previous data collected in 2008, Acinetobacter baumannii resistance against carbapenems increased to 35.9% in 2017 (Abdulrazzaq, N.D; AlKaabi et al., 2011; Thomsen & Abdulrazzaq, 2019). Nevertheless, based on 2018 data, resistance against carbapenem has declined to 32.8% which was contradictinganother figure mentioned in the same document (35%). Additionally, Acinetobacter baumannii showed high resistance rate against almost all antibiotics such as ciprofloxacin (40%) and Ceftazidime (42%) (Thomsen, 2019).

In the official report published by the Ministry of Health and Prevention (MOHAP) in UAE in 2021, Acinetobacter Spp resistance against carbapenem showed a decline to 25% based on data collected in 2019. Furthermore, the pathogen demonstrated reduced resistance against almost all antibiotics tested. On a similar note, the MDR strains for Acinetobacter Spp showed reduction across the years from 49% in 2010 to 25% in 2019. However, the absolute sensitivity figures for Acinetobacter baumannii were still low for several antibiotics such as imipenem, meropenem and piperacillin/tazobactam (74%, 75% & 70% respectively) (National Sub-Committee forAMR surveillance, 2021).

The report also highlighted the declining trend for resistance of Acinetobacter Spp. Across the years from 2013 to 2019 against the major antibiotic classes as carbapenems, cephalosporins, fluroquinolones, aminoglycosides and penicillins (National Sub-Committee for AMR surveillance, 2021). Finally, as mentioned earlier, reduction of the MDRO infections (including Acinetobacter baumannii) due to antimicrobial stewardship program in one of UAE hospitals was confirmed but without breakdown data (Sadeq et al., 2021).

Overall, resistance was increasing from Acinetobacter Spp against different groups of antibiotics (especially carbapenems) from 2008 till 2018 (Sonnevend et al., 2013; Thomsen, 2019). In 2019, resistance started to show decline against carbapenems and other agents. Furthermore, MDR prevalence reduced compared to previous years. However, the absolute figures for Acinetobacter Spp susceptibility againstdifferent types of antibiotics was still low (National Sub-Committee for AMR surveillance, 2021).

Pseudomonasaeruginosa

Pseudomonas aeruginosa (P. aeruginosa) resistance level has increased from 2004 till 2008. Even during 2008, resistance against several antibiotic classes such as aminoglycosides, cephalosporins and fluroquinolones has increased as well.

Resistance level for P. aeruginosa against carbapenem (imipenem) reached 19.6% in 2008 (AlKaabi et al., 2011).The period from 2008 till 2015 has no data available on resistance pattern for P. aeruginosa. Data that were collected during 2015 and 2016 revealed the carbapenem resistant P. aeruginosa estimated at 23.9%. Bearing in mind the multiple mechanisms for resistance, P. aeruginosa is considered as a challenging and one of the important pathogens in UAE especially with the presence of VIM/GES-9 co-resistance gene. P. aeruginosa resistance to piperacillin/tazobactam was 43% and for imipenem/meropenem was 81% (Moubareck et al, 2019).

Two years later in 2017, resistance level against carbapenem matched the one announced in 2008 at a percentage equal to 19.7% (Abdulrazzaq, N.D; Thomsen & Abdulrazzaq, 2019). Reduction in resistance against carbapenem continued to reach 16.2% in 2018 while its sensitivity against piperacillin/tazobactam improved to be 87% in the same period. Similarly, susceptibility to other antibiotics enhanced such as aminoglycosides and cephalosporins (Thomsen, 2019).

Finally, the resistance pattern for the pathogen based on 2019 data showed continued reduction to be 14.4%. P. aeruginosa resistance decline from 2010 to 2019 was against almost all antibiotics except fluroquinolones that was increasingand cephalosporins that was at plateau. Absolute susceptibility in 2019 was quite acceptable for all antibiotics especially for aminoglycosides. Even MDR P. aeruginosa level has declined from 22% to 17% in the period from 2010 to 2019 (National Sub-Committee for AMR surveillance, 2021).

In conclusion, P. aeruginosa resistance was increasing from 2008 till 2017 against several antibiotics especially carbapenems (Abdulrazzaq, N.D; AlKaabi et al., 2011; Thomsen & Abdulrazzaq, 2019). Starting from 2017, the resistance pattern declined gradually against the same antibiotics. Moreover, MDR strain prevalence was declining as well. Even the absolute susceptibility figures were acceptable for most of the antibiotic classes. The only exception was fluoroquinolones that the pathogen maintained its resistance against it (National Sub-Committee for AMR surveillance, 2021; Thomsen & Abdulrazzaq, 2019).

Non-TyphoidalSalmonella(NTS)

One of the pathogens that has high importance grading is Non-Typhoidal Salmonella (NTS) (National Sub-Committee for AMR surveillance, 2021). NTS resistance against fluroquinolones has been estimated during 2012 at 13.2% (WHO, 2014).This percentage has surged to 18.9% in 2017 (Abdulrazzaq, N.D: Thomsen & Abdulrazzaq, 2019). Furthermore, the percentage reached a resistance level of 39.5% in 2018 (Thomsen, 2019). After increasing pattern recorded till 2018, considerable reduction in resistance has been observed in 2019 at 18.5%. Elevating pattern of resistance has been noted against other classes as well such as cephalosporins, aminopenicillin and MDR (National Sub-Committee for AMR surveillance, 2021).

In closing, NTS resistance against fluroquinolones was increasing remarkably till 2018 (Abdulrazzaq, N.D; Thomsen, 2019; WHO, 2014). Sharp decline in resistancestarted in 2019 against the same class. While against other classes, increasing trend has been observed (National Sub-Committee for AMR surveillance, 2021).

Shigellaspp.

WHO report published in 2014 provided interesting data regarding Shigella spp. resistance across the globe including UAE. Susceptibility level for Shigella spp against fluroquinolones has been stated as 89.8% based on 2012 data (WHO, 2014). In 2017, elevation of resistance has been witnessed for the pathogen that extended to 22.2% (Abdulrazzaq, N.D; Thomsen & Abdulrazzaq, 2019). Surprisingly, the resistance pattern almost has doubled to 42.9% in 2018 (Thomsen, 2019).

Slight reduction to 42.1% has been recorded in 2019 (National Sub-Committee for AMR surveillance, 2021). To summarize, except for slight reduction in 2019, resistance pattern was increasing for Shigella spp against fluroquinolones from 2012 till 2018 (National Sub-Committee for AMR surveillance, 2021; Thomsen & Abdulrazzaq, 2019; Thomsen, 2019; WHO, 2014).

Neisseriagonorrhoeae

Neisseria gonorrhoeae susceptibility against Cephalosporins (third generation) has been documented by WHO in 2014 in different regions in the world. However, there was no data available related to this pathogen in UAE (WHO, 2014). Similarly, in 2017 there was no data available regarding sensitivity to Cephalosporins. However, data on Neisseria gonorrhoeae resistance against fluroquinolones has been documented to be 74% (Abdulrazzaq, N.D.).

The trend continued increasing in 2018 to reach 81.2% (Thomsen, 2019). Finally, in 2019, the resistance reached its maximum scale to 91.4% against fluroquinolones (National Sub-Committee for AMR surveillance, 2021). In conclusion, although limited data, Neisseria gonorrhoeae resistance against fluroquinolones wasincreasing steadily in the last 3 reports (Abdulrazzaq, N.D; National Sub-Committee for AMR surveillance, 2021; Thomsen, 2019).

Vancomycin-resistantEnterococcusfaecium(VRE)

Among the high importance pathogens is VRE (National Sub-Committee for AMR surveillance, 2021). VRE prevalence revealed to be 8.1% in 2017 (Abdulrazzaq, N.D.). Although the rate of MDRO infections (including VRE) reduced from 2015- 2017, breakdown data was not available to evaluate contribution of VRE (El Lababidi et al., 2019). VRE strain maintained spreading to attain prevalence of 11.5% in 2018. Additionally, VRE demonstrated high resistance rate for ampicillin, levofloxacin and moxifloxacin (77.9%, 76.2% and 75.5% respectively) (Thomsen, 2019).

However, in 2019, VRE declined relatively to 10%. Resistance trend from 2010 to 2019 for Enterococcus faecium against antibiotics other than vancomycin showed no significant change except for glycopeptides that declined considerably for VRE to 10%. MDR prevalence for Enterococcus faecium has been recorded to be 30% in 2019. VRE resistance against ampicillin and moxifloxacin reduced slightly to 73% for both agents in 2019 (National Sub-Committee for AMR surveillance, 2021).

In summary, VRE was increasing from 2017 till 2018 then followed by slight reduction in 2019 (Abdulrazzaq, N.D.; Thomsen, 2019). VRE showed high resistance for other antibiotics as well such as beta-lactams and fluroquinolones. Nevertheless, Enterococcus faecium resistance against antibiotics other than vancomycin did not change significantly (National Sub-Committee for AMR surveillance, 2021).

Streptococcuspneumoniae(S.Pneumonia)

Another pathogen with medium importance was Streptococcus pneumoniae (S. Pneumonia) (National Sub-Committee for AMR surveillance, 2021). S. Pneumonia showed resistance level of 12.9% against penicillin based on data collected in 2012(WHO, 2014). Data from 2013 till 2016 was not available. However, in 2017, S. Pneumonia resistance surged remarkably to reach 59.6% against the penicillin G in particular (Abdulrazzaq, N.D.).

Thomsen (2019) study demonstrated the decline in resistance to 50.7% in 2018 data against the oral penicillin. However, this percentage was apparently lower for intravenous formulation at 5.6%. Nevertheless, discrepancy in the same document was evident as resistance to penicillin has been stated to be 3%. Susceptibility has been shown to be as low as 52% and 58% for erythromycin and tetracycline respectively (Thomsen, 2019).

Reliable figure can be extracted from the official report for MOHAP that highlighted the resistant rate at 11.8% against the oral penicillin (42.7% in meningitis) in 2019. However, resistance in non-meningitis was as low as 3.1%. From 2010 till 2019, the resistance pattern was recorded to be decreasing against beta-lactams while increasing for almost all other classes. Moreover, MDR percentage was increasing in 2019 to reach 44%. In summary, S. Pneumonia resistance was decreasing against beta-lactams while increasing against other classes as macrolides, sulfamethoxazole/trimethoprim, flurouquinilones and MDR (National Sub-Committee for AMR surveillance, 2021).

Haemophilusinfluenzae(H.influenzae)

The data on H. influenzae resistance in UAE remain limited. However, in 2017, H. influenzae resistance against ampicillin was reported at percentage of 9.3% (Abdulrazzaq, N.D.). Moreover, resistance level was elevated in 2018 to reach 14.9% against same agent (Thomsen, 2019). The resistance pattern continued to expand during 2019 for H. influenzae to be 27.3% against ampicillin. In addition, H. influenzae displayed high resistance against amoxicillin/clavulanic acid and sulfamethoxazole/trimethoprim (23% and 26% respectively). However, ciprofloxacin maintained its efficacy with susceptibility level of 98% against the pathogen (National Sub-Committee for AMR surveillance, 2021).

OtherPathogens

Most of the selected articles focused on the main pathogens with clinical importance (critical, high and medium importance). However, few articles or reports discussed the resistance patterns of other less important pathogens (National Sub-Committee for AMR surveillance, 2021). Stenotrophomonas maltophilia was one of the less important pathogens that was discussed with resistance level increasing before 2008 till reach the highest level in 2008 at percentage 11.3% against sulfamethoxazole/trimethoprim (AlKaabi et al., 2011).

Pathogen resistance for the same antibiotics continuously increased to 13% in 2018. Additionally, Stenotrophomonas maltophilia had low sensitivity rate for ceftazidime equal to 65%. Minocycline was the only agent remained effective against Stenotrophomonas maltophilia at level of 95% (Thomsen, 2019).

Clostridioides difficile is one of the pathogens that was out of the priority list and has been discussed in one of the articles (National Sub-Committee for AMR surveillance, 2021). Infections related to Clostridioides difficile reduced significantly to 0.12 case/one thousand patient days in 2017 due to antimicrobial stewardship program implemented (El Lababidi et al., 2019). However, in 2020-2021, stewardship program implemented did not improve infection rate for pathogen. On the contrary, more cases of Clostridium difficle have been identified in the intervention group (Sadeq et al., 2021).

A dissertation paper (Ph.D) discussed the rate of tuberculosis in UAE published in 2018. The paper has showed that there was no major change (only slight reduction) in tuberculosis rate from 2012 to 2015. Additionally, there was a slight reduction in MDR from 15.12% to 7.69% in the same period. Similarly, tuberculosis resistance to antibiotics slightly decreased over time to 0.6% (using culture test). Isoniazide had the highest resistance level at 8.8% followed by streptomycin (8.5%), Pyrinzinamide (7.6%) and rifampicin (5.4%). Although Ethionamide showed high resistance (40%) but the sample size was low to consider this figure into account (Al Hosani, 2018).

Other less important pathogens have been mentioned in few reports/documents but without enough data to be evaluated in this report. Examples for these pathogens include Morganella morganii, Citrobacter koseri, Enterobacter cloacae, Proteus mirabilis, Serratia marcescens, Klebsiella oxytoca and others (National Sub-Committee for AMR surveillance, 2021; Thomsen, 2019).

Limitation

This paper is the first systematic review to discuss the impact of ASP in UAE on bacterial resistance level in the last few years (according to the best knowledge of the researcher). The research covered several databases in searching for articles. Additional strength for this paper is that grey literature, governmental websites and hand search were approached to ensure that publication bias has been avoided (Paez, 2017). Furthermore, critical appraisal and scoring system have been used to assess the quality of included papers objectively (Brice, 2020; JBI, N.D.). Finally, evaluation of each pathogen separately in chronological manner (from the oldest to the newest publication) allowed for traceability of resistance in a trend approach.

However, this paper has few limitations as well which mandate interpreting its data cautiously. First, not all relevant databases have been searched due to accessibility issue. Second, as Google scholar shows only 1000 articles from the search results, search has been made on 3 consecutive timeframes which created discrepancy in number of articles found (Harzing, 2010). Additionally, the online library for the university of ESSEX has been used in the search which might not be accessible for all researchers who plan for reproducing the research.

Moreover, there was no evidence that all the sites used for isolates collection in the selected articles were applying ASP at the time of the study (or even it was not known if they were applying before or after isolates collection except for 2 studies only). Regarding the 2 studies that were assessing ASP impact, MDRO and MRSA were declining after ASP implementation while ESBL was increasing. Both studies were focusing mainly on cost issue and antibiotic consumption rather than resistance trend in sufficient details (El Lababidi et al., 2019; Sadeq et al 2021). Accordingly, causality relationship could not be established between ASP implementation and resistance pattern change (Saks & Allsop, 2019). Finally, it was not possible to obtain local data/reports from local hospitals or the national antimicrobial stewardship committee directly which would have been valuable addition to the research.

Furtherresearch

Evidence detailing the evaluation of ASP in UAE is scarce. Further research in this area is required to assess the impact on bacterial resistance. In addition, only one official surveillance report is published (National Sub-Committee for AMR surveillance, 2021). Additional reports are required as well more frequently. Futureresearch on bacterial resistance should be representative and include several sites from different emirates.

One of the main recommendations is to have a universal system for the ASP and surveillance covering the whole country. In addition, process should be institutionalized rather than being person-dependant. Moreover, alignment between different sectors is required to adopt “One Health” approach (UAE Higher Committee for Antimicrobial Resistance, 2019).

Addressing these requirements will help in generating more representative data and support research efforts. Finally, implementing ASP across the entire country and regular evaluation for resistance (rather than cost and general clinical outcomes only) will enable to trace and curb resistance.

Conclusion:-

Antimicrobial resistance elevation is a major issue in UAE (National Sub-Committee for AMR surveillance, 2021). Consequences of the antimicrobial resistance are diverse and vast including cost, morbidity and mortality (Antimicrobial Resistance Collaborators, 2022). In addition, it enforces the healthcare system to use alternative medications that may pose risk of tolerability concerns for the patients (CDC, 2021a).

The aim of this systematic review was to identify the bacterial resistance trend against major antibiotics in UAE in the period 2007 to 2022 especially after implementing surveillance system in 2010 in Abu Dhabi (followed by rest of the country in 2015) (National sub-committee for AMR surveillance, 2021). Additionally, the study was aiming to identify the gaps in the antimicrobial stewardship programmes applied in country.

Bacterial resistance showed a remarkable increase against several antibiotic classes in UAE from 2010 till 2021. Collectively, except for minor decline in 2019 and low rate in 2021, MRSA prevalence was increasing steadily across the years from 2002 till 2019 (Thomsen, 2019; National sub-committee for AMR surveillance, 2021). Similarly, Enterobacteriaceae resistance was increasing steadily until 2015 mainly driven by E. coli rather than K. pneumonia. However, later, resistance of K. pneumonia started to increase slowly, and XDR rate showed a high percentage.Additionally, MDR rate was increasing for both E.coli and K. pneumonia until 2019. Except for a slight decline in 2019, ESBL was spreading continuously across the entire period from 2008 to 2019.

On a different note, resistance level of Acinetobacter Spp started to increase before 2008 (AlKaabi et al., 2011). Even in 2008, data confirmed reduced susceptibility of Acinetobacter baumannii to all antibiotics except colistin with remarkable increase in MDR and XDR prevalence (Sonnevend et al., 2013). High resistance for the pathogen has been supplemented with data confirming high prevalence of genes responsible for difficult type of resistance among Acinetobacter baumannii strains (Zowawi et al., 2015). Data collected during 2017 showed the continued increase in resistance that declined in 2018 (Thomsen & Abdulrazzaq, 2019; Thomsen, 2019).

The decline in resistance against carbapenem continued to decline in 2019 to reach the lowest level since many years (25%). Additionally, the resistance against other antibiotics and prevalence of MDR reduced as well. However, the absolute resistance level is still high considering different classes of antibiotic. Moreover, data from last report showed declining pattern for the resistance in the last 6 years (2013- 2019) which is contradicting with previous publications. Nevertheless, as the lastreport is the official one from MOHAP (other documents was not structured reports or studies), results from this report dominated other documents (National Sub- Committee for AMR surveillance, 2021).

Other than that, before 2008, susceptibility of P. aeruginosa was declining against almost all antibiotics. This surge in the resistance continued to occur in 2008 (AlKaabi et al., 2011). Similarly, same pattern of increase was observed during 2015- 2016 (Moubareck et al, 2019). However, in 2017 the resistance level against carbapenem started to decline (Abdulrazzaq, N.D; Thomsen & Abdulrazzaq, 2019).

Identical pattern of decline has been observed in 2018 against variety of antibiotics including carbapenems and penicillins for both P. aeruginosa and MDR (Thomsen, 2019). The lowest carbapenem resistance has been recorded in 2019 for the pathogen. In addition, absolute susceptibility for all antibiotics tested was relatively accepted (National Sub-Committee for AMR surveillance, 2021).

However, discrepancy between the last report published in 2021 and previous data need to be considered. The last report highlighted the decline in resistance from 2010-2019 without details for the period in-between (National Sub-Committee for AMR surveillance, 2021). While the previous publications describe the resistance pattern as increasing till 2017 then started to decline. For example, if it would have been drawn as a graph it would be plotted as a bell shape graph.

However, NTS data showed variability regarding resistance against different classes. Resistance against fluroquinolones was increasing from 2012 to 2018. While in 2019, there was a remarkable decline in resistance. On the contrary, resistance against other classes such as cephalosporins and MDR was increasing(Abdulrazzaq, 2019; National Sub-Committee for AMR surveillance, 2021; Thomsen, 2019).

Shigella Spp was one of the pathogens that showed consistent elevation in resistance against fluroquinolones from 2012 to 2018 with slight reduction in 2019 (National Sub-Committee for AMR surveillance, 2021; Thomsen, 2019; WHO, 2014). Similarly, Neisseria gonorrhoeae resistance against fluroquinolones has increased steadily from 2017 to reach its maximum level at 91.4% in 2019 (Abdulrazzaq, N.D; National Sub-Committee for AMR surveillance, 2021).

Variable resistance level has been documented for VRE against vancomycin and other antibiotics as well. VRE prevalence increased from 2017 to 2018 but reduced slightly in 2019 (Abdulrazzaq, N.D; Thomsen, 2019). Enterococcus faecium resistance against antibiotics other than vancomycin did not change significantly from 2010 to 2019 except for glycopeptides that reduces considerably. Moreover, VRE against ampicillin and moxifloxacin has not shown any major difference in 2019 compared to previous year. However, absolute resistance figures against most antibiotics remained high (National Sub-Committee for AMR surveillance, 2021).

Surprisingly, S. Pneumonia resistance was decreasing against beta-lactams while increasing against other classes as macrolides, sulfamethoxazole/trimethoprim, fluroquinolones and MDR (National Sub-Committee for AMR surveillance, 2021).

Navigating through the resistance pattern for H. influenzae, it showed increasing trend from 2017 to 2019 against ampicillin and in 2019 against amoxicillin/clavulanic acid. However, ciprofloxacin was restoring its activity against H. influenzae in the same year (National Sub-Committee for AMR surveillance, 2021).

The paper also discussed resistance pattern for other pathogens such as Stenotrophomonas maltophilia that was increasing against sulfamethoxazole/trimethoprim from 2008 to 2018 continuously (AlKaabi et al., 2011; Thomsen, 2019). Likewise, its resistance against ceftazidime was high in 2018 (Thomsen, 2019).

Moving to a different pathogen which is tuberculosis, there was slight reduction in rate of infections, resistance to antibiotics and MDR rate from 2012 to 2015 (Al Hosani, 2018). Unfortunately, no more data was available to assess the resistance pattern in other years. Besides, Clostridium difficle infection rate showed fluctuation in 2 different studies after implementing antimicrobial stewardship programs. In 2017, the pathogen showed decline in infection rate which increased in 2020-2021 in the intervention group. There was no data mentioned concerning Clostridium difficle resistance against antibiotics in both studies (El Lababidi et al., 2019; Sadeq et al., 2021).

Regarding evaluation of the antimicrobial stewardship programs, only 3 articles from the selected articles were discussing this point. Unfortunately, the focus for 2 of these papers was assessing cost and antibiotic consumption rather than resistance pattern. Accordingly, there was insufficient data on impact of intervention on resistance pattern (El Lababidi et al., 2019; Sadeq et al., 2021). The first study showed reduction in both MDRO and Clostridium difficle infection rate (El Lababidi et al., 2019).

Similarly, the second study showed reduction in MDRO and MRSA in the intervention group. However, ESBL and Clostridium difficle infection rate increased (Sadeq et al., 2021). The third document was an action plan rather than resistancesurveillance report which was lacking data on resistance (UAE Higher Committee for Antimicrobial Resistance, 2019).

Gaps in antimicrobial stewardship program and surveillance system in UAE include lack of national reference laboratory (National Sub-Committee for AMR surveillance, 2021). In addition, there was inequality in efforts and focus directed to different emirates. Moreover, work should be institutionalized rather than being person- dependant. Furthermore, the gap in antimicrobial stewardship programs has been attributed also to several conditions such as overlap between ASP and IPC, being applied in only few medical affiliates and lack of enough research to guide actions.

Finally, “One Health” approach should be followed to ensure alignment between different stakeholders from different sectors (UAE Higher Committee for Antimicrobial Resistance, 2019).In conclusion, there was a considerable effort has been made to establish surveillance system and ASP since many years in UAE. However, ASP in UAE remains in need for improvement through filling the gaps mentioned above.Generally, bacterial resistance is increasing widely in UAE since 2007. Several pathogens have showed steady increase in resistance across all the years covered (except with slight reduction in the last year/s) such as Enterobacteriaceae, MRSA, ESBL, Neisseria gonorrhoeae, Shigella spp, VRE and H. influenzae.

However, other pathogens showed increased resistance in the beginning followed by decline in the last few year/s such as P. aeruginosa, NTS (against fluroquinolones only) and Acinetobacter baumannii (absolute resistance level remain high). On the contrary, S. Pneumonia had declining resistance trend against beta-lactams across all years while increasing resistance pattern against macrolides and fluroquinolones.Likewise, tuberculosis showed slight decline in resistance against antibiotics. Consequently, this pattern of resistance from priority pathogens and gaps in ASP mandate an action from stakeholders in UAE to curb the resistance problem.

Finally, there was no evidence that the sites (hospitals and medical centres) involved in the studies selected were implementing ASP or not at the time of the study. Even if there was an ASP established, data was not available to confirm whether this program was implemented before or after sample collection except for 2 studies.Even, these 2 studies were not focusing on bacterial resistance with enough details (El Lababidi et al., 2019; Sadeq et al 2021).

Accordingly, causality relationship between impact of ASP and bacterial resistance level cannot be confirmed. Rather, association between ASP and resistance can be considered (Saks & Allsop, 2019).

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