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Bachelor's Thesis

HOSPITAL ACQUIRED INFECTIONS: FOCUS ON MRSA AND VRE

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ABSTRACT

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The purpose of this study was to investigate how to prevent hospital acquired infections caused by MRSA and VRE. Hospital acquired infections is becoming a threat to the health sector across the world. The study was meant to provide answers to the following three research questions:

1. What is prevalence of MRSA and VRE infections from a global perspective.
2. What are the major risk factors associated with Hospital acquired infections caused by MRSA and VRE.
3. What are the possible preventive or control measures that could be applied in the Finnish hospitals.

The study was approached from the world perspective to European level and narrowed down to Finland. It provides answers to the above mentioned research questions and Systematic literature review was used as a data analysis method. Nineteen journals from thirteen countries were included in the research work, Finland inclusive. Two tables were drawn to show details of the articles involved, details about the purpose of the articles, authors, year of publication and authors' opinions.

Key words: Hospital infections, Bacteria, transmission agent, MRSA, Antibiotics resistance, preventive measures, MRSA and VRE risk factors, epidemiology, prevalence,

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1. INTRODUCTION

My interest towards hospital acquired infection as a research topic was developed over a period of time, mostly during my nursing academic pursuit. Hospital was expected to be the safest zone for the patients but interaction with the outside society shows that many still see hospital as reservoir of infections, and considered it unsafe for the patients. This situation boosted my observation and curiosity during my various clinical practices, both in Finland and outside Finland. To really explore detail about Hospital acquired infections and how they can be managed, I decided to dedicate my bachelor thesis to this study.

From a broader view, hospital acquired infections can be caused by bacteria, virus, fungi, prions, viroids and parasites. To avoid explosion of ideas, streamlining the topic to focus on infections related to MRSA and VRE was considered. MRSA and VRE are microorganisms that belong to the class of Bacteria. They are common infections all over the world and have ability to cause countless number of infections in the hospitalized patients.

In this study, prevalence of MRSA and VRE are generally described from a global level and narrowed down to Finnish level. Infection epidemiology in relation with management in different countries was analyzed, compared and cogent objectives were derived. In the end, control and preventive measures suitable for Finnish hospitals are drawn out. Systematic literature review method was used to explore the useful information considering different research articles were involved. Efforts were made to figure out the relevant articles systematically to arrive at a more precise and reliable conclusion.

2. BACKGROUND

Over the past twenty years, the incidence of infections caused by antimicrobial-resistant pathogens has increased dramatically across the world, especially in vulnerable high-risk population, such as patients in intensive care unit (ICU), burns unit and the immuno-compromised people. This has raised a serious global concern among the general public, health officers, patients and the relatives.

2.1 MRSA and VRE

Infections could be described as the detrimental presence of foreign species (pathogens) in a host. The word pathogen covers viruses, prions, bacteria fungi, parasites and viroids. The capacity of a microorganism to cause disease is referred to as pathogenesis (Wilson 2000). The infecting pathogen multiplies at the expense of the host and interferes with the host's normal functioning system. In the other hand, hospital acquired infections (HAIs) are the infections developed while being hospitalized, however, not all acquired infections develop during hospital stay, some colonize the healthy people in the community. In this case, they are called community acquired infections (CAIs). Recent studies have suggested that infections caused by MRSA can be acquired outside healthcare settings in the community (Kerttula et al. 2004). These infections have different infection sites, the overwhelming majority of CO-MRSA infections are skin and soft tissue infections, whereas HA-MRSA infections were primarily postoperative wound, respiratory tract, or bloodstream infections (Faria et al. 2004.)

Problem of clinical recognition led to a conclusion that when an infection is acquired within 48 hours of patients' admission, it can still be considered to be community acquired infections because there is high probability of being brought from the community by the patients. Besides having established itself in the hospital setting, is now beginning to appear in the wider community as well as among people without typical associated risk factors for MRSA acquisition (Velazquez-Meza et al. 2004.)

Both micro-organisms could give rise to infections and colonization, CA-MRSA is capable of causing infections in otherwise healthy people and may have a serious or even fatal outcome (Faria et al. 2004.)

MRSA was first identified in the United States in 1968 (Herwaldt 1999) at Boston city hospital, USA. It was detected sporadically in Europe in 1961 (Michel & Gutman 1997). Different years of identification in different countries were noticed around the world but the fact is that they exist and they are significant in the health sector. Existence of MRSA in different countries has had a negative impact on the hospital. MRSA has remained a major cause of nosocomial disease worldwide, causing 50% or more of hospital acquired Staphylococcus aureus infections in several countries (Faria et al. 2004).

MRSA and VRE are bacteria that resist methicilin and vancomycin treatment respectively, but in the recent time, they were referred to as multidrug-resistant due to their resistance to a large group of antibiotic. Certain multidrug-resistant bacteria have become endemic in the hospital environment, particularly in the intensive care units, chiefs among these are methicilin-resistant staphilococcus and vancomycin resistant enterococci (Handerson 2006).

A number of countries have witnessed one epidemiology or the other in their respective hospitals while some continue living with these infections. The incidence of MRSA and VRE continue to increase in most health care facilities despite the efforts of infection control programs over the last 30 years (Burger et al. 2006). Staphylococcus aureus is one of the most important bacteria causing disease in humans and most commonly identified antibiotic-resistant, also, hypothesized to colonize animal. MRSA account for 30% to 50% of all nosocomial infections in some US hospitals (Kotilainen et al. 2003). MRSA is as well noted to be the most common cause of skin and soft tissue infections like Abscesses, carbuncles, folliculitis, furuncles, impetigo, bullous impetigo and cellulitis. MRSA has a largely clonal structure due to low frequency of recombination between Staphylococcus.

The distinct pandemic lineages have been named Iberian, Brazilian, Hungarian, New York/Japan, Pediatric, and EMRSA-16 clones, and the identification of clones was based primarily on a combination of PFGE, PCR-based techniques.

In the other hand, enterococci are bacteria that live in the gastrointestinal tract of most individuals known as colonization and the common ones are commensal organisms in the human intestines (Herwaldt 1999). Generally, they do not cause any harm or injury. Enterococci are gram-positive cocci that often occur in pairs (diplococci) or short chains and are difficult to distinguish from streptococci physically. They do not really require oxygen for their metabolic activities but can survive in oxygen-rich environment. Its exact origin is unknown, but *van*A and *van*B gene clusters are likely the products of a complex evolutionary sequence of genetic transfers (Bradley 1999.)

In the late 1980s, VRE emerged as important pathogens in the hospital setting and recently, pan-resistant gram-negative bacilli have become increasingly prevalent (Edmond et al. 2008). Enterococci are not as familiar as staphylococcal or Escherichia coli bacteria, they are among the most common type acquired by hospitalized patients e.g mostly patients in the intensive care. Enterococci in general, are much less capable of causing diseases than staph or E. coli but still can complicate and prolong hospital stay. Important clinical infections caused by enterococcus include urinary track infections, diverticulitis, meningitis, bacteremia, bacterial endocarditis and many more. These organisms cause infections and colonization, colonized patients are not easily detectable by some diagnostic methods, therefore, colonization stands chance of becoming infection later**.** Boyce noted that in hospitals with MRSA prevalence, 30%-60% of patients who become colonized with MRSA will acquire a subsequent infection with that organism and these infections cause significant morbidity and mortality (Herwaldt 1999)**.**

2.2 Epidemiology

This part is to present information about infection rate of MRSA and VRE in the hospital, how they develop and spread among patients and healthcare workers. According to Webster's new world medical dictionary, reservoir of infections is any person, animal, plant, soil or substance in which an infectious agent normally lives and multiplies. Considering the growing and infection rate of MRSA and VRE on a global scale, hospital remain the main reservoir of these infections, however, community also harbour these infections to some extent. In the hospital, a number of things can be regarded as reservoir of infections and from which these infections spread easily. These reservoirs are patient's body system (throat, wound, rectum, nares etc); healthcare workers and hospital environment (including dry surface because MRSA and VRE can survive for months on a dry surface). First detected in hospitals in the 1960s, methicillin resistance is now increasingly recognized in the community (Lowy 2003.)

MRSA and VRE pose problems to the health sectors due to their ability to spread among the patients and healthcare workers, they have distinct features of surviving on a dry surface for months. Endemicity and pandemicity of a particular disease depends on how faster it can spread; its adaptive features, which make it possible for causative organism to develop resistance towards antibiotics. More so, their possibility to survive for days or months outside living hosts (including dry surface areas) has to do with their adaptive features. Developing resistance towards all antibiotics has really shaken the physicians. In 1992, 19,000 deaths directly caused by nosocomial infections made them the eleventh leading cause of death in the US population (Harrison 1998). In 1997, the first report of vancomycin intermediate resistant staphylococcus aureus (VISA) came from Japan, and additional cases were subsequently reported from other countries (Lowy 2003). Meanwhile, methicilin introduction in 1961 was rapidly followed by reports of methicillin-resistant isolates (Lowry 2003.)

Over the last four decades, hospitals in the United States have seen a progressive increase in the proportion of staphylococcus aureus isolates that are resistant to methicillin from less than 3% in 1975 to 64% in 2003 (Edmond et al. 2008). In the article of Michel & Gutmann (1997), enterococcus was ranked as the second most common agent of nosocomial infections for 1986 to 1989. MRSA and VRE epidemiology are different, depending on countries, noted to be low in some countries and higher elsewhere.

Higher in countries like USA, UK, Portugal and Taiwan compare to Switzerland, Denmark, Netherlands and Finland, where strict control measures like proper hygiene, active screening, isolation contact, less antibiotic consumption etc have been properly followed. Proportion of MRSA causing Staphylococcus aureus bloodstream infection is higher in the UK, Ireland, Portugal and Greece than in most other European countries (Humphreys 2005). MRSA remains a particularly serious problem in Portugal because of the alarming high incidence and multidrug resistance of the strains (Aires et al 1998). In Denmark, a national surveillance system of staphylococcus disease has been in operation at the statens serum Institut since the late 1950s and strict infection control introduced during the 1970s have kept the incidence of MRSA infections extremely low in Denmark (Faria et al. 2004.)

However, elderly people of age 65 and above normally have immuno-compromised body system which makes them to be more susceptible to invading microorganisms. MRSA cases notified to the NIDR rose from 120 in 1997 to 597 in 2002 (from 2.3 to 11.5 cases per 100 000 population), the increase was greatest in elderly people and outside Helsinki metropolitan area (Kerttula, Lyytikäinen & Salmenlinna 2004). Most people in this category of age are common in Nursing homes, which is another reason that indicates that, there is high chance of epidemic occurrence from nursing homes. In many countries, nursing and residential homes with endemic MRSA have been responsible for spreading this microorganism into the neighboring hospital (Kotilainen et al 2001). Meanwhile, most of the epidemics that broke out and cut across hospitals and nursing homes in different countries, mostly, have their origin affiliated with the hospitals but further spread may be aided by the nearby nursing homes and residential homes.

2.3 Prevention of MRSA and VRE in hospital setting

Harbouring sites in a patient are throat, wounds, rectum, nares etc. They may also colonize the face, hands, axilla, or groin, but their primary habitat is the epithelium of the anterior nares (Henderson 2006). Colonization with staphylococcus aureus predominantly occurs at four sites: the nares, the skin, the rectum, and the perineum (Bradley 1999). These areas can be heavily colonized or infected, mostly in chronically ill patients.
Therefore, sharing a room or any device with this kind of patient could possibly lead to spread of disease, especially a patient with compromised body immunity. Colonization with MRSA is often asymptomatic, without any symptoms, asymptomatic Staphylococcus aureus colonization can occur in 10%−20% of healthy persons (Bradley 1999). In the other hand, colonization increases the risk of infections which may serve as a reservoir for transmission to other patients (Henderson 2006). Risk factors surrounding the chance of being colonized are diminished functional status, open wounds, antibiotic therapy and presence of foreign bodies in the body system (e.g. nasogastric tubes, intravenous catheters and urinary catheters). These risk factors are similar to those identified in patients in acute care facilities.

It has not been an area of interest, for many years, to conclude that healthcare workers are part of reservoir of infections in an hospital. Detail analysis and updates show that healthcare workers, who engage in patients' care, stand risk of carrying these organisms on their hands or by medical tools. Various studies conducted in different countries reported a positive relationship between antimicrobial use and incidence of MRSA colonization or infection within the hospital setting (Henderson 2006). The efforts to come up with new drugs have been in futile due to resistive feature. However, genotype analysis of MRSA hospital isolates confirmed the existence of epidemic clones with great capacity to spread and get adapted to hospital environments. Over time, bacteria naturally acquire chromosonmal mutations or acquire genetic material from other organisms in their environment that confer resistance to anti-bacterial drugs (Henderson 2006).

Many hospitals in different countries have witnessed epidemiology of MRSA and VRE, which has really cost inconveniences, large sum of money and loss of lives.

Research work is being carried out on a daily basis, in a move, to develop a permanent solution that could arrest the situation but distinct adaptive features of these micro-organisms have made it so difficult for the efforts to succeed. Due to emergence of resistance to various antibiotics, in the early 1970s, physicians were finally forced to abandon their belief that, given the array of effective microbial agents, virtually all bacterial infections were treatable (Lowy 2003).

Moreover, some patients are more prone to infections than the others or some conditions make them to be more susceptible to infections. Infection may ensue in the presence of some inciting event, such as a surgical procedure or underlying disorder like diabetes or the need for dialysis (Bradley 1999). For microbes to cause infections in the body system, it needs to gain entrance into the body system as they are not harmful to the intact skin. However, they can remain active and stay longer on intact skin but can only become detrimental when they find their ways like as wounds and surgical sites, into the body system. Underlying disorder weakens the immunity of the body, this is known to be medical conditions of the elderly and common features in acute care. A colonized patient stand high chance of becoming infected, meanwhile, identifiable risk factors for MRSA colonization include diminished functional status, presence of foreign bodies (e.g., nasogastric tubes, intravenous catheter, urinary catheters), open wounds, antibiotic therapy, and prior MRSA colonization (Bradley 1999.)

Another set of people that fall into this category of re-infection possibility are previously treated or admitted patients, in an epidemic-witnessed hospital. There is high probability that they carry the infections during epidemic crisis. Sharing devices or rooms with an infected person has led to series of epidemic in many countries, especially people on oxygen support. These days, over use of these drugs are making the microbes to be tougher to control. Antimicrobial resistance prolongs the duration of hospitalization, thereby increasing the cost of patient care (Aires et al 2001). This is the reason why physicians are becoming stingy in prescribing antibiotics to the patients, even if the patient is in need of it. Being admitted in the intensive care units expose a patient to the risk of contacting these infections as most of the ICU patients are suffering from serious underlying complications which is responsible for their easy susceptibility to infections.

According to Kotilainen et al. (2003), majority of the 39 patients who acquired the medical strain, during 1990s Finnish epidemic crisis, had severe underlying diseases. Sharing room or any other thing with this type of patient can easily lead to cross-infection.

Apart from contaminated instrument and environment, Patient or healthcare workers' transfer is another risk factor that has contributed to the outbreak in some countries. Healthcare workers are not normally screened while on transfer to another hospital, meanwhile some patients seems to be healed are not subjected to receiving followed-up assessment. Kotilainen et al (2003) came up with the observation that MRSA patient was placed in a single room to be cared for in contact isolation, but when the wound healed, the patient was transferred to a three-bed room. subsequently, three of his roommates acquired MRSA. Normal control procedures are hand hygiene, protective clothing, use of gloves, proper disposal etc. Difficult-to-adopt ones are professional sensitive and refer to as aggressive measures in most cases. They are normally used collectively when the epidemic situation is becoming uncontrollable. Mostly, they are conducted by the infection control professionals. In any outbreak, the first line of action seems to be active surveillance culture, to identify the carrier, colonized and infected patients.

To control MRSA in the hospital setting, many advocated for a ´´Search & Destroy´´ strategy which involves performing active surveillance for MRSA by culturing patients on hospital admission and periodically (Clinical Microbiology Newsletter 2008). This is an acclaimed infection control strategy behind low prevalence in Netherland, known to have adopted by Finland, UK and USA in the past. This strategy has also attracted criticism, pointing to its disadvantages, being too expensive to adopt and requires significant resources. The effectiveness of ASC-CP to control MRSA in the setting of high endemicity, however, remains unclear, and a great debate has ensued in the hospital epidemiology community (Clinical Microbiology Newsletter 2008). Early discharge can also play an important role. Most patients with MRSA are discharged back to the community and, with decreasing length of stay, more after care is performed in primary care, early discharge of patients with MRSA forms part of most national guidelines (Maudsley et al 2094).

Moreover, it takes 1-5 days especially when a BEC is used (Kluytmans 2007). This brings about unnecessary keeping patients in isolation rooms, who may end up not carrying the microbes. In a country like Netherland with a low level of this infection, approximately 95% of these patients will not carry MRSA (Kluytmans 2007). Patients in isolation rooms are deprived of enjoying Doctors' and Nurses' attention compare to others who are in the general wards. This is tendency of developing depression if this continues. Though, isolation system has helped in controlling outbreak. Meanwhile, possibility of a patient being colonized up to 4 years indicates that keeping such patient in isolation would be so difficult for hospitals with fewer resources.

Efforts are made to limit the active surveillance to certain number of patients with clear suspicion of carrying MRSA or VRE microbes and use of economic method, purposely to minimize the cost and reduce unnecessary isolation delay. A rapid diagnostic and less expensive test like PFGE is required. Several major different pandemic MRSA clones have been identified mainly by PFGE ie Iberian, Brazilian, Hungarian, New York/Japan, Pediatric and UK EMRSA-15 and -16 clones (Kerttulla et al. 2007). In an outbreak situation, if an infected person is discovered in a shared room, all other members are screened, if discovered in a ward, the whole ward is screened. The minimum screening sites include nostrils, wounds and exit sites of devices (Kerttula et al. 2007). Failure of a test to detect presence of micro-organism normally leads to a serious pandemic.

Laboratory test failed to identify the carrier of MRSA and was later detected in a Dutch hospital after 2yrs (Kluytmans 2007). This led to a serious epidemic in Netherland which involved more than 50,000 screened patients and despite an intensive approach, it took more than a year to control the outbreak (Kluytmans 2007). It was proposed that a new patient or a transferred patient from abroad should be screened before granting admission but seems to be beyond reach of certain hospitals. Resistance to antibiotic happens to be another problem, the noticeable rise of MRSA and VRE was significantly correlated with the increased consumption of glycopeptides, B-lactam-B-lactamase inhibitor combinations, extended-spectrum cephalosporins, carbapenems and fluoroquinolones (Hsueh, Chen, Teng & Luh 2005).

Discharging of MRSA carriers is to remove the potential reservoir and put a stop to the spread but this seems not be a feasible practice. UK incorporates discharge of MRSA carriers as part of their National Infections guidelines and studies shows it has not been contributing to high rate CO-MRSA. Eradication involves discharge MRSA carriers; decolonize MRSA carriers; disinfect the environment (Bradley1999). Disinfecting the environment helps but many a times environmental and patients' strain may not be genetically similar. Few studies done in Nursing homes reveal that environmental MRSA strains may not necessarily correlate with the strains known to colonize patients (Bradley 1999.)

The issue of developing national guidelines for hospital infection control seems not to be a thing of importance to many countries few years back. In Denmark, a national surveillance system of staphylococcal disease has been in operation at the Statens Serum Institut since the late 1950s (Faria et al. 2004). In comparism, National Guidelines for the control of MRSA in Finland were prepared in 1995 after 1991-1992 outbreaks. One of the Infection control strategies employed in approaching 1991-1992 Finnish epidemic situation was a Dutch idea known as Search & Destroy. This same method was also adopted in UK and USA due to its efficiency but later replaced with a more flexible ones following continuous high prevalence.

With the dramatic increase of MRSA, other countries (including the United States) where these microbes are already endemic in hospitals, have adopted more flexible control policies (Kotilainen et al. 2003). It signifies that each country's situation determines the kind of applicable method. Healthcare staffs need updated knowledge of infection control in other to function well in an epidemic crisis. After the 1990s epidemic crisis in southwestern Finland, Kotilainen (2003) observed that the factors possibly contributing to our success include active education and excellent compliance of health-care personnel; a uniform health-care system and low population density.

3. AIMS AND RESEARCH QUESTIONS

Aims of a research work is an important aspect of a study, efforts were made to set out some questions which are to be answered by the study following the intensive reviews of the materials. This study is to provide answers to the research questions and ability of the study to provide adequate answers to the set questions, would justify its validity and reliability. Below are the research questions.

1. What is the prevalence of MRSA and VRE infections from a global perspective.

2. What are the associated major risk factors.

3. What are the possible preventive or control measures that could be applied in the Finnish hospitals.

4. SYSTEMATIC LITERATURE REVIEW

4.1 Method

The method employed in this study is Systematic literature review (S.R). What do we mean by systematic review and how does it fit-in into my study? In the first case, the nature of this study is to process the past or existing researches to answer the set research questions. Systematic review uses existing primary research for secondary data analysis**.**

In a situation where large volume of data is involved, S. R helps in controlling the data in a logical way and make use of all the relevant information that evolved. Randomized controlled trials related to a particular question are identified systematically, and methods used to identify studies are reported in full (Brophy et al. 2008). Most of the time, it is preferable to try S. R for a study before embarking on a fresh study. There may not be need to conduct a new study anymore. S.R are recommended before designing a new study because they can identify weaknesses in the methodology of existing studies and may prevent unnecessary replication (Neale 2009). Systematic literature views systematic review from a very broad angle as a method with the following features : a clearly defined research question; transparent methods, defined a priori to include clear criteria for including and excluding studies; exhaustive searches for published and unpublished studies; explicit reporting of the methods used to appraise, abstract and synthesize information from individual studies, conducted in duplicate to minimize errors; and clear presentation of study findings.

The increasing volume of researches introduces systematic review into the world of research findings and it has been contributing immensely in the way of bringing the existing researches to a usable form. S. R is a time consuming approach, tiring, even more than new study, but it allows series of ideas to come into play for analysis and comparism. In the end, the study looks more factual than new study because facts are borrowed from the past researches and these facts are not directly lifted from the main source but refined in a better way.

From another angle, systematic review is described as easy to underestimate the time and resource required to conduct a systematic review. Each stage requires much painstaking work, and a review is likely to take months, rather than weeks (Neale 2009).

Statistical feature of S. R makes the results of S. R to be more reliable and valid. It allows possibility of using mathematical approaches which helps in drawing a significant relationship among the data under study. A particular advantage of systematic review including a meta-analysis is their statistical power (Neale 2009). Clearly defined research questions in the beginning of a study give a direction to the systematic review method. S. R has a logical way of providing answers to an already set research question, it follows the analysis in a chronological order till the end and arrives at the answer. It also creates a room for future modification. Having a clearly defined research question is fundamental to the success of a systematic review (Neale 2009).

4.2 Review process

The nature of this research work demanded for a kind of review method. In the beginning, an effort was employed to extract information from academic search engines. Public search engines were involved but in the process, most articles that are not rooted in academic databases were lacking relevant references, quality and reliability. Due to this, the line of search was changed and narrowed down to academic search engines alone such as Sciencedirect, Ebesco, ebrary etc but the mission to retrieve a quite number of articles still holds. With this streamlining of search engines, the broadness of the initial topic still made the search to be too explosive to handle and there is need to narrow the topic itself the more.

The topic underwent series of reformation process to arrive at the usable form. At this stage, the search was becoming controllable and functional search terms were developed. Year of publication of an article shows the recency of a study is and the target was articles from 2000 till date. This seems to be unrealistic as many of the articles were prepared in the 1990s.

Therefore, the need to widen the range and articles prepared below year 2000 became a necessity. Less strict limitations was set in the key words, to accommodate unexpected relevant materials to set in during the search. MRSA, VRE and Prevention & control were made as major key words while others such as risk factors, epidemiology, hospital acquired infections, colonization, transmission agents were used as minor The name MRSA and VRE themselves are derived from the word "resistance to antibiotics". Therefore, the word resistance and antibiotics need to be made as important key word as well.

Moreover, after general selection of the available articles, 34 research articles were recovered. Three of the articles are laboratory studies about MRSA and VRE genes, mainly genetic issues. They are deeply rooted in genetics and too complex to be connected with the research topic, they are therefore removed. Another four articles concentrate their efforts either on MRSA or VRE in relation to Nursing homes. Meanwhile, the plan is to use only one article that treat nursing home as the main subject. Four articles on nursing homes are not needed and decided to pick the one done in Finland, not only because it is a Finnish study but due to the ability of the article to incorporate various nursing homes and health center wards, that are in one way or the other, in relation to past Finnish epidemic. The same idea was also used to remove three articles that have to do with MRSA, VRE and Community, leaving two articles that contribute to this topic from the angle of community prevalence.

The focus of the thesis is to view the topic from the world perspective, considering ranges of articles across the world and narrow it down to Finland as a country. For this motive to hold, articles to be considered have to be distributed round the world. In the accepted articles, about Eleven (11) of them are conducted in USA, though they have the needed information while contents of some other are repetition of another. To create room for articles from other countries and prevent redundancy of US articles, six of US articles were considered and four articles are considered from Finland. In the end, only nineteen articles from 13 countries remain vital.

4.3 Data Analysis

This section is meant to present information about the main idea of all the nineteen accepted articles, their focus; how they were conducted; results of the findings; year of publication and their relationship with the thesis. To avoid going out of the track in the literature analysis, there was a focus on the main idea of each article and how they can provide answers to the research questions. Six studies conducted in the United States are from different cities, this is just to allow inflow of ideas from different geographical locations. About five of these articles focused on managing MRSA. Aires de sousa (2001) shows comparism assessment among five countries in Latin America concerning MRSA clone. Justification of argument was made one of the priorities in this study, comparism here and there led to consideration of similar articles. These articles were made use of as they inter-connect the epidemiology and infection control at the international level.

All the nineteen articles have deep study or related issues to do with MRSA while only six of them include VRE as part of their main headlines and eight other articles treat VRE as sub-topic in their contents. Altogether, about fourteen articles treat VRE as either main topic or sub-topics out of twenty one articles and with these fourteen articles, balance is noticed in the study. Apart from the prevention and control discussion in the content of seventeen articles, seven studies make prevention, control, therapy, managing, eradicating and elimination as part of their main headings.

Seven articles from the following European countries: Denmark, France, Netherland and Finland base their research studies on epidemiology. Two of the Finnish articles concentrated their studies on the same thing but one limit its major study on Turku University hospital. Turku University Hospital happened to be the main source of the 1990 epidemic among the affected hospitals and nursing homes. Meanwhile, the second one gave extensive detail about Mynamaki Health Center epidemic and its surrounding nursing homes in connection with the same epidemic. In this study, age range is not really considered as the main search criteria but content and publication year are made important to authenticate the recency.

Exclusion to this is an article that considered elderly people as the class of sample but due to compromised immunity and sedentary lifestyle, many studies argued that elderly people around 60 years or more are more proned to hospital acquired infections.

Most of the articles made use of sample materials, either collected by questioneers, interviews or data extraction, from a reliable database. It involves using the data to generate statistical tables and curves to ascertain a situation and draw a conclusive message. Six mathematical methods were used ranging from Pearson's correlation co-efficient, time series, student t test, chi-square test to least square regression. Meanwhile, some are essay-type, which incorporates use of argument and reviews in a logical reasoning. Due to the evolution of two categories, It was realized that there is need for generation of two different tables with slightly different features.

In the next page, there is structure of studies that base their results on samples. The need for comments in the table serves as the interpretation of the researchers' opinions.

ANALYSIS OF THE STUDIES

Author(s)	Aims of the research	Research sample & Place of research	Research outcomes	Year of publication and comments
Aires de Sousa et al	MRSA spread from Brazil to Portugal.	210 Isolates from 3 hospitals. Portugal	100% resistance to penicillin , methicilin, and oxacillin and 100% susceptibilities to vancomycin.	Published 1998. Its high resistance helps spreading
Aires de Sousa Marta et al.	Geographic expansion and persistence of the Brazilian clone.	499 isolates from Argentina, Brazil, Chile, Uruguay, Mexico.	Brazilian clone is found in these five countries	Published 2001. Boarder sharing may be responsible..
Burger Terry et al.	Benchmark for MRSA,VRE & CDIF.	4-year data sharing analysis.32 hospitals in New Jersey & Pennsylvania.	Downward trend in VRE and MRSA and upward trend for CDIF.	Published 2006. Standard infection control works
Faria. A. Nuno A. et al.	Analysis and classification of MRSA isolates.	105 isolates, 81 analyzed. Denmark	36 (44%) were HA-MRSA AND 45 (56%) were CO-MRSA.	Published 2004. Justifies presence of CA-MRSA & HA-MRSA despite strict infection control.
Hsueh et al	High prevalence of MRSA & VRE NTUH.	297 isolates. Taiwan	Stepwise increase of MRSA	Published 2005. Antibiotic overdose
Kerttula A.M. et al.	To examine molecular epidemiology of MRSA in Finland	1718 cases of MRSA, median age is 63 years. Finland	Annual increase is from 1.5 cases/100 000 in 1997 to 13.1 cases/100 000 in 2002.	Published 2004. steady increase on a yearly basis outside Helsinki.
Kerttula Anne-Marie et al.	. To examine molecular epidemiology of MRSA in Finland.	4026 cases of MRSA. median age is 63 years. Finland	Annual increase is from 2.3 notifications/100 000 in 1997 to 27.9 in 2004. notifications/100 000.	Published 2007. There is a sharp increase between 2002-2004.
Maudsley. J et al.	Assessing UK elderly for CO-MRSA	250 elderly people living in their own homes. UK	CO-MRSA is low in London (0.8%). Other UK surveys compared.	Published 2004. Early discharge with low CO-MRSA.
Velazquez-Meza. M. E et al	To determine MRSA clonal evolution and the influence of infection control in a Mexico city pediatric hospital (1997-2003)	Total of 659 S. aureus strains. Mexico	From 1997-2001 the rate varies between 17% & 23%; drops to 14% in 2002 and to 0% in 2003	Published 2004. Sharp reduction is observed due to intervention of infection control.

Figure 1: Description of materials

The second table in the next page represents the structural frame of the articles that base their results on argument and analysis of the opinions as regards the topic.

Author(s)	Aims of the research	Main discussions	Research outcomes/conclusions	Publication year and place
Bradley . F. Suzanne	MRSA controlled in long-term facilities	Risk factors, prevalence, outbreak and its management.	Colonization is more common in long term and standard infection control reduces transmission	Published 1999. U.S.A
Clinical Microbiology Newsletter	Search & Destroy shortcomings & alternatives.	Positive & negative sides of ASC-CP with alternative approaches.	83% reduction in nosocomial infections after ASC-CP intervention. Infection control should not be MRSA specific.	Published 2008. U.S.A
Henderson. K. David	preventing spread of nososcomial infections	Colonization, transmission, resistance, risk factors and controls	Successful prevention demands understanding the epidemiology, pathogenesis and routes of transmission.	Published 2006. U.S.A
Herwaldt. A. Loreen	How MRSA can be controlled in the Hospital	Why MRSA strains should not be accepted as normal flora.	No single best control, approach must be in line with epidemiology of the organism and available resources	Published 1999. U.S.A
Humphreys. H	Comparism of MRSA control from different countries	interventions, comparism of strategies and the contributing factors	Bed management, under-staffing, resource sharing, incompliance etc were noted as failures.	Published 2005. Ireland
Kluytmans Jan	MRSA and help of rapid diagnostic tests.	Effectiveness of S&D, Control of MRSA and active screening.	Successful control is possible with combination of active screening, contact isolation and rapid diagnostic tests.	Published 2007. Netherland
Kotilainen Pirko et al.	Eradication of MRSA from MHC and associated nursing homes	Eradication treatment; strains identification; Screening & Follow-up cultures	Eradication was successful in all the concerned patients except one dementia patient that died in contact isolation after 21 months.	Published 2001. Finland
Kotilainen Pirkko et al.	Elimination of MRSA from Turku University hospital.	Outbreak at medical, surgical& hematological units and Elimination treatment	There is possibility of controlling non-endemic MRSA with strict approaches and re-emergence is also possible.	Published 2003. Finland
Lowy. D. Franklin	Relationship between Antibiotic resistance and microbes	How microbes develop resistance to old and new antibiotics and future impact	New drugs' efficacy is doubted but MRSA can still be controlled by stricter infection control.	Published 2003. U.S.A
Michel. M & Gutmann. L	Therapeutic realities and possibilities for MRSA & VRE	Emergence of MRSA; antibiotic resistance; treatment and control options	Transfer of genetic feature is a real concern but continuous vigilance; strict preventive measures & antibiotic restrictions can limit spread.	Published 1997. France

Figure 2: Description of the materials

4.4 RESULTS

Answers are provided in this section to the following research questions:

1   Prevalence of MRSA and VRE infections from a global perspective.
2   What are the major risk factors associated with Hospital acquired infections caused by MRSA and VRE.
3   What are the possible preventive or control measures that could be applied in the Finnish hospitals.

To answer the first question, Aires et al. (2001) has it that MRSA and VRE prevalence are of high rate in Latin America (Argentina, Uruguay, Chile, Mexico and Brazil). Valazquez-meza et al. (2004) also support the Aires' view by claiming high prevalence in Mexico. High rate in USA is presented in all six studies from USA and some others from other countries such as Denmark, UK etc. Meanwhile, the only study from Taiwan by Hsueh (2005) raised the issue of highest prevalence in Taiwan. Ten out of twenty studies based their research works on Europe and covers seven countries in Europe, Finland, UK, Ireland, Portugal, France, Netherland and Denmark. Three studies relate UK, Ireland and Portugal with low prevalence, meanwhile, one study out of these three studies figure out Portugal as a country of more prevalent compared to UK and Ireland. All the Ten articles carry low prevalence about all Scandinavia countries, including Finland. Considering the above review, it is concluded that prevalence of MRSA and VRE among the considered countries occur in this order:

–   Country with the lowest prevalence is Switzerland followed by Netherland.
–   Relatively low in Denmark and Finland.
–   It is moderately high in Ireland, UK, Portugal, Greece, France and USA.
–   More higher in Latin America (Argentina, Brazil, Chile, Mexico & Uruguay).
–   The Nation with the highest prevalence is Taiwan

Answers to the second question were figured out from more than ten articles.

There are a vast number of risk factors to MRSA and VRE but the main ones are discussed on a broader scale in the literatures while the minor ones such as contaminated environment, improper hand hygiene, attitude of not wearing protective coverings etc were superficially discussed. The proven ones known to have links with MRSA and VRE infections are:

1) Previous hospitalization or previous history of MRSA and VRE
2) Presence of foreign bodies (e.g nasogastric tubes, intravenous catheters, urinary catheters)
3) Shared-rooms, -materials and -medical tools
4) Immuno-compromised body system and old age
5) Uncontrolled antibiotic consumption
6) Prolonged hospital stay

Answers to the third research question, possible preventive measures that could be applied in the Finnish hospitals, emerged in many ways in the article review.

They are brought under five major categories.
- Surveillance culture and active education
- Search and Destroy (active screening and contact isolation treatment)
- Reduction in antibiotic consumption and decreasing hospital stay
- Maintenance of staff ratio and timely decision

5. DISCUSSION

5.1 Method

Systematic literature review was employed in this study, details about the method is given in chapter four. Purpose of this section is to present how this method is used to review the articles. After gathering the valuable articles, the next line of action was to analyze the data and make use of them properly. As one of the features of systematic review, it is used to handle voluminous data. The data looks too explosive but step by step analysis drew lines of priority in-between the salient points and the same idea was used to group them into different categories. Similarity and differences of the articles were coordinated in other to understand which articles that answer a particular research question better.

In the process, there were conflicts of ideas but critical analysis showed that some ideas were mere personal and not based on clinical research works. In the end, all the data were systematically broken down and re-grouped to take care of the research questions. Though, it involved lots of time to come up with a reasonable conclusion but it made the whole analysis compact and usable.

5.2 Results

Providing answers to the three research questions, requires another idea of re-grouping all the literatures into another 3 broad categories and each category is able to provide satisfactory answers to each question. To avoid tabular redundancy, the idea was just used as a guideline without any table.

Articles in the first group based their studies mostly on epidemiology, spread and transmission which answer the first research question. The second research question was taken care of by the articles conducted on clinical investigation, assessment and surveillance exercises.

In the discussion part of nine articles, risk factors are highlighted with the support of clinical investigation and five others have it as part of their content. There is vast number of risk factors but the main ones are given priority in most of the studies. Main risk factors known to have led to most of the epidemic in the studies are associated with acute care setting but sometimes nursing homes and long term care.

 In the context of many of these articles, identifying risk factors are very important as they are one of the component that determine the kind of approach to be used in controlling epidemic situation. All four studies from Finland described previous hospitalization as an important risk factor, three of the studies associate previous hospitalization with re-colonization possibility. Idea of sharing things in the hospital setting is prohibited, though still in practice but much detail was not given about this in some of these studies. Three studies about community, long term facilities and Nursing homes, see immuno-compromised body as the main factor in hospitalized old age people. Lowy (2003) in his study, focused mainly on antibiotic resistance and gave detail on the relationship between antibiotic consumption and hospital infections. He also see antibiotic therapy as the cause of prolonged hospital stay.

Moreover, many articles on eradicating, eliminating, managing, implementing and antibiotic usage paved way for the possibility of answering the third research question on preventive measures. All control measures are found in almost twenty articles, each category was seen from different perspectives. Different ideas were used in extracting the possible preventive measures, the rate at which a strategy is used in controlling epidemic situation; how effective is the strategy and how economical it is in practicality. Surveillance culture, for example, was a point of discussion in thirteen studies and described as significant tool of detecting presence of microbes in an epidemic or non-epidemic situation. Active education was referred to as one of the needed infection control tools by seven researches. Exploration on Search & Destroy strategy gained more attention, it encompasses both active screening and contact isolation. Being an infection control idea, believed to be more efficient, more than ten studies have the same ideological views about it.

6. RELIABILITY AND LIMITATIONS

This thesis was purely based on systematic literature reviews which involve use of articles and books from academic database. All these academic materials are known to have undergone series of tests and criticism and I believe using such research materials must have made it possible for my argument to be more close to the right conclusion. Comparism of methods and ideas from several authors before making conclusion are expected to have contributed positively to making a right judgment. Fifteen out of nineteen considered researches are carried out in the year 2000 and above, which shows recency of the used articles. Meanwhile, the articles are from 13 different countries, mostly conducted by research institutions and proffessionals with comparable ideas, results and opinions.

The study is about comparing the infection control strategies in many countries, definitely, argument and biased judgment cannot be removed. An author may be using a kind of patriotic idea to hide the real picture of the epidemic situation in his or her own country. Humphreys (2005) was highly concerned about the high prevalence of MRSA and VRE in UK and Ireland, commended the Finnish efforts as regards controlling 1990s' epidemic outbreak and was later of the opinion that Finnish 1990 outbreak was possible to manage because it was not endemic enough. In so many literatures, there are conflicts of ideas cited to be right somewhere and proved to be wrong elsewhere. Therefore, it is possible that this conflict of ideas might have led to supporting my claim wrongly in some conclusions during this study.

Few studies are too old to help in making the right conclusion, four articles are more than ten year old and the situation in that country might have improved. Therefore, using such old version article may not be perfectly right to arrived at reliable conclusion. The problem of language cannot be left out in these limitations, the study deal with articles from various countries with different languages. Some important studies might have come in another language other than English. This translation problem must have deprived me of gaining access to those information. There are several places in the studies where National Infection Control Guidelines are mentioned and extract are used to explain a situation. The version of Finnish National Infection control guildelines is in Finnish, therefore, denying me of access to it in a more clearer form.

7. CONCLUSION AND IMPLICATIONS

The situation of the hospital acquired infection is becoming difficult to approach on a daily basis, despite large amount of money and professionals being invested on it. Efforts should be continuously made to suppress the microbes in the hospitals, once the situation is well managed in some countries, then, controlling it is not an impossible thing. Furuno et al (2004) says there is no simple and cost-effective methods currently exists for identifying high risk patients on admission to hospital wards outside ICU. The control efforts should continue but the responsibility of controlling HAIs rests majorly on Infection control professionals and Health care workers while patients and relatives could also be carried along in the process of preventing these infections.

Considering the broadness of this research topic, it could be described as integral part of the subject 'infection' and therefore be used as a step for the future students. Some other areas of infection can still be explored such as 'Relationship between HAIs and CAHs'. Antibiotic resistance of MRSA and VRE are discovered to be a significant aspect that contributes to the treatment difficulty of these microbes. So, another research target may be 'impact of infection control methods on the microbial resistance' and so on.to the topic being studied, though, not part of the initial set questions.

APPENDIX

NIDR   National Infection Disease Register

PFGE   Pulsed-field Gel Electrophoresis

PCR   Polymerase Chain Reaction

CDIF   Clostridium Difficile

UMMC   University of Maryland medical center

MHC   Mynamaki Health Center

NTUH   National Taiwan University

ASC-CP   Active surveillance culture with contact precaution

S&D   Search and Destroy

MRSA   Methiclin Resistant Staphiloccocus Aureus

VRE   Vancomycin Resistant Enteroccocus

HAIs   Hospital Acquired Infections

CAIs   Community Acquired Infections

S.R   Systematic Review

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