Nosocomial infection in hospital: Review

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Introduction:

Nosocomial infection is diseases acquired by patients under medical care (١).Hospital acquired infection can be define as an infection acquired in hospital by a patient who admitted for a reason other than infection. Theses infection occur in hospital during operation or during injured or burning infection also occur in medical staff in hospital (٢). Another new term called health care associated infections is refer to the type of infection occur when stay in hospital as a risk factors which may lead to death (٢).In development countries was recorded a high rate as (75%) caused by theses infection(٣). Some microorganisms in asymptomatic patients may be considered infection if microorganisms are found in found in body fluid or body site as a blood CSF or serum(٤)In hospital increased some pathogenic such as toxoplasmosis , rubella, syphilis ,CMV and appear after 2days birth due to the incubation which was acquired trans-placenttaly(٥). Hospital acquired infections (HAIs) are a major problems for low and middle-income countries which have limited healthcare resources (٦).The risk of health-care-associated infection has been estimated to be (2-20) times higher in developing countries than that of resource-rich countries with the percentage of infected patients exceeding 25% (٧).

The highest frequencies of acquired hospital infections reported from hospital in Eastern Mediterranean and South East Asia Regions are (11.8%) and (10.0%) respectively (٨). Nosocomial infections increase the costs of healthcare due to added antimicrobial treatment and prolonged hospitalization. Since the prevalence of nosocomial infections is generally higher in developing countries with limited resources, the socio-economic burden is even more severe in these countries (9). Hospital acquired infections (HAI) present a serious problem in patient safety, resulting in increased mortality rates, prolonged hospital stays, and higher costs (10). According to the World Health Organization, a Hospital acquired infection is an infection acquired in hospital by a patient who was admitted for a reason other than that infection (٦). This review summarizes the current knowledge on the risks of HAI.

Types of nosocomial infections:

Some types of acquired infections include central line associated bloodstream infections, catheter-associated urinary tract infections, surgical site infections and ventilator-associated pneumonia as the following types:

2.1. Central line-associated bloodstream infections (CLABSI) :

A central line-associated bloodstream infection is Known as a laboratory-confirmed bloodstream infection not associated with an infection at another site that develops within (48)hr of central line placement. More cases are preventable with aseptic techniques, surveillance, and management strategies.(١١) .It is more dangerous or deadly nosocomial infections with death cases rate (12–25)% (١٢).Catheters are placed in central line to provide fluid and medicines but prolonged use can cause serious bloodstream infections resulting in compromised health and increase in care cost (١٣). Although there is a decrease of (46%) in CLABSI from (2008–2013) in United States hospitals yet an estimated (30,100) CLABSI still occur in intensive care unit (ICU)and acute facilities wards in united states each year . The most frequent types of infections include central line related with bloodstream infections, catheter joined with urinary tract infections, surgical site infections and ventilator-associated pneumonia(١٤).

2.2. Catheter associated urinary tract infections (CAUTI):

The most common hospital-acquired infections in humans is urinary tract infections and caused primarily by some mainly bacteria as uropathogenic Escherichia coli .Biofilm of bacteria was occur in Indwelling urinary catheters which was resisted to some type of antibiotics, biofilm related in catheter associated with urinary tract infections, and it lead to chronic infection (15). Catheter made from rubber, plastic or silicone and some types of catheters as, indwelling catheter that resides in the bladder and it is also called Foley catheter(16).CAUTI is called as a symptomatic patient with a urinary catheter wih one or more symptoms or signs, as fever or temperature at (38°)C. A dysuria or suprapubic tenderness, with positive urine culture with no more than two pathogens isolated (17) .Mortality cases in Europe, rate of nosocomial infections is (10- 97)% which was related to catheters. About (80%) of nosocomial urinary tract infections are associated with indwelling urinary catheters. Antimicrobial resistant can cause recurrent and chronic infections and if untreated it may cause acute or chronic pyelonephritis, bacterial vaginosis, chronic prostaitis, bacteraemia and death (18). The most risk factors for CAUTI as age, diabetes requiring insulin therapy, long hospitalization and long duration of catheter

insertion (19) . Staphylococcus aureus (MRSA), *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Proteus mirabilis* and *Staphylococcus epidermidis* are the main urinary pathogens that cause biofilm related urinary tract infections and considered as Causative Organisms of Catheter associated Urinary tract infection in Medical Wards and Intensive Care Units (16).Biofilm formation by some bacteria that protects pathogens from host immune defense and antimicrobial agents is the leading cause for CAUTI. The use of antimicrobial coating for urinary catheters in the past few years, was demonstrated to be one of the most direct and efficient strategies to reduce infections (20)The impact of a UTI on the individual can vary greatly, depending on age, co-morbidities and socio-economic circumstances. CAUTIs may lead to unnecessary use of antibiotics and antimicrobial resistance and longer hospital stays (21). CAUTI is caused by instrumentation of the urinary tract and has been associated with increased morbidity, mortality, hospital cost, and length of stay. Urinary tract infection associated with catheterization may be extraluminal or intraluminal. Extraluminal infection occurs via entry of bacteria into the bladder along the biform that forms bacteria around the catheter in the urethra. Intraluminal infection occurs due to urinary stasis because of drainage failure (22).

2.3. Surgical site infections (SSI): Surgery related with nosocomial infections by rate (2–5)% of patients. It regarded as a second most common type of nosocomial infections mainly caused by some bacteria as *Staphylococcus aureus* resulting in prolonged hospitalization and risk of death (23). The pathogens causing SSI arise from normal flora of the patient. The incidence may be as high as (20%) depending upon procedure and surveillance criteria used (24). The term surgical wound infection was replaced by surgical-site infection by Task Force in 1992 to include infections of organs or spaces deep in the skin and soft tissues. Centre for Disease Control (CDC) divided a surgical-site infections in united states into superficial incisional SSI, deep incisional SSI, and organ space SSI (25). Both gram-positive and gram-negative bacteria play a role in infection of surgical wounds (26). *Staphylococcus aureus* was recorded a high rate (31.58%) and followed by *Klebsiella pneumonia* (26.31%), *Pseudomonas aeruginosa* (15.79%), *Escherichia coli* (10.53%), *Acinetobacter spp*(10.53%) and *Proteus mirabilis* (5.26%) .These bacteria was a problem for surgeons because regarded as multi-drug resistant bacteria Postoperative SSIs was a lethal, remaining as a less mortality but in surgical patients was a major source of morbidity(27). Some factors affecting the infection rate as skin preparation, wound contamination, the length of pre-operative hospital stay, drainage of wounds, age of the patient,

duration of surgery, and skill and technique of the surgeon. There is higher infection rate involving senior surgeons, which can be attributed to the fact that they perform more difficult and lengthy surgeries, while the low rate of infections in surgeries performed by medical officers can be attributed to the fact that they perform simpler and uncomplicated surgeries (27).

2.4. Ventilator associated pneumonia (VAP) VAP It is nosocomial pneumonia found in (9–27)% of patients on mechanically assisted ventilator. It usually occurs within 48 h after tracheal incubation (28). Nosocomial pneumonia is associated with ventilation with rate (85%)(29).Fever, leucopenia, and bronchial sounds are common clinical manifestation in VAP (30). Another name of VAP is Nosocomial respiratory tract infections are major causes of extreme morbidity and mortality in United States of America hospitals, affecting about (5-10). Bacterial pneumonia percentage (25%) of all ICU infections. Ventilated acquired pneumonia is the highest in the initial course of hospital stay. The mechanical ventilation increases the risk of nosocomial respiratory infections .Two factors associated with respiratory tract infection is decreased immunity, and colonization of human cavities by bacteria (31). Mechanical ventilation, lymphocytopenia, sepsis, ICU admission on first day, older age and anemia were a risk factors that predispose patients with severe influenza A as a nosocomial infection (32). Aspiration of nose and throat secretions is thought to be the most important cause of nosocomial respiratory infections, and dental plaques can also cause it (33). *Acinetobacter baumannii, Pseudomonas aeruginosa, Stenotrophomonas maltophilia, and Staphylococcus aureus* is a Nosocomial respiratory tract infections bacteria (32). Nosocomial respiratory infections can be treated with erythromycin or fluoroquinolone for cases of legionellosis. Some antibiotics as amoxicillin with clavulanic acid, ceftazidime, imipenem, and piperacillin was used for treatment also (31).

Nosocomial skin and soft tissue infections :

some sign and symptoms was associated with Nosocomial infections affecting the skin and soft tissues, like pain, edema, warmth, erythema, , cutaneous blood loss, skin sloughing, skin anesthesia, rapid evolution, and gas in the tissue (34). Skin and soft tissue infections (SSTIs) result from invasion of the skin, and mostly occur due to trauma or surgery. SSTIs can be classified as simple, necrotizing or suppurative (35). Risk factors of acquiring SSTIs include older age, diabetes mellitus, immune-compromise, alcohol abuse, and prolonged hospitalization. SSTI was infected and increased in man than female (36). *Staphylococcus aureus,*

Pseudomonas aeruginosa, Enterococcus, and Escherichia coli are commonly isolated from inpatients associated with SSTIs.

Agents of nosocomial infections: Nosocomial infections are caused by different microorganisms as bacteria are responsible for (90%) but protozoans, fungi, viruses and mycobacteria are less than bacterial infections (26). The bacterial agent in nosocomial infection like *Streptococcus spp., Acinetobacter spp., enterococci, Pseudomonas aeruginosa (P. aeruginosa), coagulasenegative staphylococci, Staphylococcus aureus (S. aureus), Bacillus cereus (B. cereus), Legionella spp* and Enterobacteriaceae family genus like *Proteus mirablis, K. pneumonia (Klebsiella pneumonia), Escherichia coli (E. coli), Serratia marcescens*. Out of these *enterococci, P. aeruginosa, S. aureus* and *E. coli* the most important role in nosocomial infection (27). UTI contain *E. coli*, while *S. aureus* is frequent at other body sites and rarely causes UTI. In blood-borne infections, coagulase-negative *S. aureus* is the main causative agent. Surgical-site infections contain *Enterococcus spp.,* which was less prevalent at respiratory tract. One tenth of all infections are caused by *P. aeruginosa*, which is evenly distributed to the entire body sites(18). The distribution of bacteria in nosocomial infections is changing over time. For example, *Proteus spp., Klebsiella spp. and Escherichia spp*. were responsible for nosocomial infections in the 1960s, but from 1975 to 1980s, *Acinetobacter spp*. with *P. aeruginosa* created clinical difficulties (27).

Nosocomial central nervous system infections :

Central nervous system (CNS) are associated with increased morbidity and mortality (60). These infections can rise from superficial wounds, foreign bodies (ventricular shunts), and the deep structures of the brain parenchyma. Most of nosocomial CNS are from bacterial meningitis and CNS shunt infections (37). About (40%) of bacterial meningitis infections are nosocomial, and Gram-negative bacilli *Haemophilus influenza* (38). Nosocomial CNS infections can be divided into surgical or device-related, and non-surgical related infections. *Mycoplasma hominis* is an atypical pathogen that have been reported in the literature as a microorganism that causes nosocomial meningitis after surgical procedure in the brain(39-40)*Escherichia coli, Klebsiella spp, Pseudomonas spp, Acinetobacter spp, Enterobacter spp, and Serratia* spp. Other bacteria which was caused a nosocomial meningitis included *Staphylococcus aureus*, coagulase negative *Staphylococci spp, Streptococcus pneumonia*, and other *Streptococci spp* (41). *Corynebacterium spp, Propionibacterium, Haemophilus, Listeria, Bacillus, Clostridium, Neisseria, Yersinia, Mycobacteria, Cryptococcus, and Ascaris* have a capability to cause nosocomial shunt infections (37). CNS infections caused by pathogens with a reduced sensitivity to drugs are a therapeutic challenge, for

instance, infections caused by penicillin-resistant Pneumococci, methicillin resistant Staphylococci, multi-resistant Gram negative aerobic bacilli, or several other organisms, including *Aspergillus spp*., *Nocardia asteroids*, which was affect primarily the CNS in immunocompromised patients. Some antimicrobials as isoniazid, pyrazinamide, linezolid, metronidazole, fluconazole, and some fluoroquinolones were used for the treatment of CNS infections (42). In children, antibiotics with good CNS penetration are intrathecal gentamicin and penicillins. Cephalosporins as cefuroxime, ceftriaxone, cefotaxime,

Nosocomial Bloodstream Infections Nosocomial :

Bloodstream infection (BSI) is a principal infectious hurdle among seriously ill patients (13). BSI acquired in the ICU are associated with significant morbidity and mortality. ICU infection preventions are including chlorhexidine body wash, central line bundles, and hand hygiene interventions (٢٣). BSI occurred in closed to 85% of patients. *Enterococcus spp* (14%) and *Klebsiella spp* (14%) were the most common organisms, and those patients with BSI had higher comorbidity scores and were more likely to be male, ill, on immunosuppression, and had a central venous catheter in place (٢٨). It has been reported that certain surgical or medical procedures may increase the probability of BSI (٢٩). The effect of nosocomial bloodstream infections on mortality, length of stay, and hospital costs in older adults was studied. A greatest percentage of BSIs were central line related and *Staphylococcus aureus* was the most common pathogen with rate (34.6%) of type of Nosocomial infection(٣٠)

Table(1):Pathogenic associated with type of nosocomial hospital infection

Type of nosocomial	Frequency	References
Blood stream Nosocomial infection	***Enterococcus spp,*** ***Klebsiella spp*** ***Staphylococcus aureus***	**17,20**
Skin and soft tissue Nosocomial infection	***Streptococcus pyogenes*** ***Streptococcus spp*** ***Klebsiella pneumonia***	**24,26**
Urine tract catheter nosocomial tract	***E.coli*** ***Klebsiella spp***	**46,47**

	Pseudomonas spp ***Enterococcus spp***	
Respiratory tract pneumonia nosocomial tract	***S. matlophilia*** ***Staphylococcus aureus*** ***Ecoli*** ***A. baumannii*** ***Klebsiella pneumonia***	**52,58**
Central nervous system nosocomial infection	***H. influenza*** ***Klebsiella spp*** ***Aspergillus spp*** ***Nocordia asteroids***	**61,67,69**

3. Nosocomial pathogens

In Nosocomial pathogens , the genus *Staphylococcus spp* is composed of several species of which *S. aureus* is responsible for diseases of acquired hospitals infection A common nosocomial bacterial agents, selected antibiotic resistant nosocomial pathogens, and source, transmission, risk factor and prevention of hospital acquired infections. Types of Nosocomial Infections Based on clinical and biological criteria, CDC and National Healthcare Safety Network (NHSN) categorize health care *Salmonella spp* associated infection sites into (23) major types which contain approximately 50 potentially specific infection sites for surveillance purpose. The most common types of nosocomial infections that could occur in a hospital set up are: Surgical wound and other soft tissue infections, urinary tract infections (UTI), Respiratory infections, Gastroenteritis and Meningitis. However, with increased use of invasive procedures for therapeutic and diagnostic purposes, cancer chemotherapy, immunotherapy and advances in organ transplants, it is possible to observe change in the distribution of nosocomial infection sites over time. Agents of Nosocomial Infections A large number of microorganisms are responsible for hospital infections and any microbe may have the capacity to cause an infection in the hospitalized patients. 90 percentage of the NIs is caused by bacteria, whereas mycobacterial, viral, fungal or protozoal agents are less commonly involved. The bacteria that commonly cause nosocomial infections include *Staphylococcus aureus*, *Streptococcus spp*.,

Bacillus cereus, Acinetobacter spp., coagulase negative staphylococci, *enterococci spp, Pseudomonas aeruginosa*, Legionella and members of the Enterobacteriaceae family such as *Escherichia coli, Proteus mirabilis,., Serratia marcescens* and *Klebsiella pneumonia.* But the most frequently reported nosocomial pathogens have been *E. coli, S. aureus, enterococci spp* and *P. aeruginosa*(43). According to the data, *Escherichia coli* and *Staphylococcus aureus* were the most commonly isolated nosocomial pathogens. Although *E. coli* is found in a quarter of urinary tract infection (UTI) cases, it is isolated relatively infrequently from other infection sites. S. aureus is rarely isolated from UTI but is common at other sites(44). It is the primary cause of lower respiratory tract infections and surgical site infections and the second leading cause of nosocomial bacteremia, pneumonia, and cardiovascular infections. The armamentarium of virulence factors of S. aureus is extensive, with both structural and secreted products playing a role in the pathogenesis of infections(45).

Epidemiology : In the developed countries (5- 15)% of hospitalized patients affected by hospital acquired infection (HAI) and it founded as many as (50%) (46) .The rate of HAI was higher in the developing countries (47) but as mentioned above, the true incidence of HAI is ambiguous in these regions.13 Mortality The HAI upraises both hospital and ICU mortality.(48). (Januel J *et al*.,2010) found 14.6% mortality for ICU- acquired HAI which was 6.1%, 3.2%, 1.7%, and 0.0% for specific site infection: pulmonary infection, central venous catheter infection, bloodstream infection and urinary tract infection, respectively(48).(Reunes *et al.*,2011) suggest bedridden and increasing age as independent risk factors for death in elderly ICU acquired BSI(49). In a trial for evaluation, the mortality of HAI according to Foglia et al report that crude mortality rates in patients infected with antibiotic- resistant organisms were greater than those infected with antibiotic- susceptible organisms. 50- Lopes et al. found in their trial that the predictive factors for mortality related to NI in pediatric was undergoing invasive procedures and the use of two or more antibiotics(51).

51. Lopes JM, Goulart E, Siqueira AL, Fonseca IK, Brito MVd, Starling CE. Nosocomial infections in brazilian pediatric patients: using a decision tree to identify high mortality groups. Brazilian Journal of Infectious Diseases. 2009; 13(2): 111-7.

References:

(1)- Krishna Prakash S. Nosocomial infection-an overview. [Online] Available from: http://www.researchgate.net/publication/18951524_ Nosocomial_infections_an_overview [Accessed on 10th October, 2014]
Benenson AS (1995): Control of communicable diseases manual, 16th edition. Washington, American Public Health Association .
(2)- Brusaferro S, Arnoldo L, Cattani G, Fabbro E, Cookson B, Gallagher R, et al. Harmonizing and supporting infection control training in Europe. J Hosp Infect 2015; 89(4): 351-6.
(3)Obiero CW, Seale AC, Berkley JA. Empiric treatment of neonatal sepsis in developing countries. Pediatr Infect Dis J 2015; 34(6): 659-61.
[4] Murray PR, Rosenthal KS, Pfaller MA. Medical microbiology. 5th ed. Missouri: Mosby Inc; 2005.
[٥] Festary A, Kourí V, Correa CB, Verdasquera D, Roig T, Couret MP. Cytomegalovirus and herpes simplex infections in mothers and newborns in a Havana maternity hospital. MEDICC Rev 2015; 17(1): 29-34.
[٦] Khan, S.A. (2009) Nosochromial Infections: General Principles & the Consequences, Importance of It's Control and an Outline of the Control Policy—A Review Article. Bangladesh Medical Journal, 38, 60-64. http://dx.doi.org/10.3329/bmj.v38i2.3576
[٧] Mayon-White, R.T., Ducel, G., Kereseselidze, T., et al. (1988) An International Survey of the Prevalence of HospitalAcquired Infection. Journal of Hospital Infection, 11, 43-48. http://dx.doi.org/10.1016/0195-6701(88)90164-8.
[6] Rezende, E.M., Couto, B.R., Starling, C.E., et al. (1998) Prevalence of Nosocomial Infections in General Hospitals in Belo Horizonte. Infection Control and Hospital Epidemiology, 19, 872-876. http://dx.doi.org/10.2307/30141571
[٨] Grimes, D.A., Peterson, H.B. and Rosenberg, M.J. (1982) Sterilization-Attributable Deaths in Bangladesh. International Journal of Gynecology & Obstetrics, 20, 149-154. http://dx.doi.org/10.1016/0020-7292(82)90029.
[9]-Raka, L. (2009) Lowbury Lecture 2008: Infection Control and Limited Resources Searching for the Best Solutions. Journal of Hospital Infection, 72, 292-298. http://dx.doi.org/10.1016/j.jhin.2009.03.017
[10]- Saint, S., Chenoweth, C., Fendrick, A.M.: The role of economic evaluation in infection control. Am J Infect Control 2001; 29: 338-344.
11-Hallam C, Jackson T, Rajgopal A, Russell B. Establishing catheter-related bloodstream infection surveillance to drive improvement. J Infect Prev. 2018 Jul;19(4):160-166. [PMC free article] [PubMed]
12- Vital signs: Central line–associated blood stream infections – United States, 2001, 2008, and 2009. Morb Mortal Wkly Rep 2011; 60(08): 243-8.

13-WHO. Preventing bloodstream infections from central line venous catheters. Geneva: WHO; 2016. [Online] Available from: http:// www.who.int/patientsafety/implementation/bsi/en/ [Accessed on 10th August, 2016]

14-CDC. Bloodstream infection event (central line-associated bloodstream infection and non-central line-associated bloodstream infection). Atlanta, Georgia: CDC; 2015.

15-Amoolya Narayanan etal, Inhibition and Inactivation of Uropathogenic Escherichia coli Biofilms on Urinary Catheters by Sodium Selenite, International Journal of Molecular Sciences, June 2018.

16- Klevens RM, Edwards JR, Richards Jr CL, et al. (2007): Estimating health care-associated infections and deaths in US hospitals, 2002. Public health reports, 122:160-166.

17- Zielinski MD, Kuntz MM, Polites SF, et al. (2015): A prospective analysis of urinary tract infections among elderly trauma patients. The journal of trauma and acute care surgery, 79:638-642.

18- Moulton L etal; J Maternal Fetal Neonatal Med. 2018-Feb; (3)395-400.

19- Muramatsu K etal, (2018), Efficacy of Antimicrobial Catheters for Prevention of Catheter Associated Urinary Tract Infectionin Acute Cerebral Infarction, J Epidemiol. 2018 Jan 5; 28(1): 54-58. doi: 10.2188/jea.JE20170022. Epub 2017 Oct 25.

20- Zhu Z, Wang Z, Li S, Yuan X. Antimicrobial strategies for urinary catheters. J Biomed Mater Res A. 2019 Feb; 107(2): 445-467. doi: 10.1002/jbm.a.36561.

21- Hatachi T, Tachibana K and Takeuchi M (2015): Incidences and influences of device-associated healthcare associated infections in a pediatric intensive care unit in Japan: a retrospective surveillance study. J Intensive Care, 3:44.

22- Tatham M, Macfarlane G, MacRae M, et al. (2015): Development and Implementation of a Catheter.

(23)- Anderson DJ. Surgical site infections. Infect Dis Clin North Am 2011; 25(1): 135-53.

24-Owens CD. Surgical site infections: epidemiology, microbiology and prevention. J Hosp Infect 2008; 70(Suppl 2): 3-10.

25-Pal N, Guhathakurta R, Al-Jumaily E, Al-Mudallal N, Muhimen N, Al-Shaibany A: Surgical site infection in surgery ward at a tertiary care hospital: the infection rate and the bacteriological profile. J Pharm. 2012, 2:1-5.

26- Sharan H, Misra AP, Mishra R: Determinants of surgical site infection in rural Kanpur, India . J Evol Med Dent Sci. 2012, 1:921-928.

27. Nichols RL, Florman S: Clinical Presentations of Soft-tissue Infections and Surgical Site Infections. The University of Chicago Press, 2001. 10.1086/321862
28- Hunter JD. Ventilator associated pneumonia. BMJ 2012; 344: 40-4.
29- Steven M, Koenig JDT. Ventilator-associated pneumonia: diagnosis, treatment, and prevention. Clin Microbiol Rev 2006; 19(4): 637-57.
30- Hjalmarson DEC. Ventilator-associated tracheobronchitis and pneumonia: thinking outside the box. Clin Infect Dis 2010; 51(Suppl 1): S59-66.
31. Blot S, Koulenti D, Dimopoulos G, et al. Prevalence, risk factors, and mortality for ventilator-associated pneumonia in middle-aged, old, and very old critically ill patients. Crit Care Med. 2014;42:601-9.
32. Zhou F, Li H, Gu L, et al. Risk factors for nosocomial infection among hospitalised severe influenza A(H1N1)pdm09 patients. Respir Med. 2018;134:86-91.
33. Terpenning M. Geriatric oral health and pneumonia risk. Clin Infect Dis. 2005;40:1807-10.
34- Stevens D L, Bisno a L, Chambers H F, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014;59:e10-52.
35- Ramakrishnan K, Salinas R C, Agudelo Higuita N I. Skin and Soft Tissue Infections. Am Fam Physician. 2015;92:474-83.
36- Ki V and Rotstein C. Bacterial skin and soft tissue infections in adults: A review of their epidemiology, pathogenesis, diagnosis, treatment and site of care. Can J Infect Dis Med Microbiol. 2008;19:173-84.
37- Morris A and Low D E. Nosocomial bacterial meningitis , including central nervous system shunt infections. Infect Dis Clin North Am. 1999;13:735-50.
38- Durand M L, Calderwood S B, Weber D J, et al. Acute bacterial meningitis in adults. A review of 493 episodes. N Engl J Med. 1993;328:21-8.
39- Zhou M, Wang P, Chen S, et al. Meningitis in a Chinese adult Downloaded from ibbj.org at 23:27 +0430 on Saturday March 27th 2021Nosocomial Infections 81 Int. Biol. Biomed. J. Spring 2018; Vol 4, No 2 patient caused by Mycoplasma hominis: a rare infection and literature review. BMC Infect Dis. 2016;16:557.
40- Whitson W J, Ball P A, Lollis S S, et al. Postoperative Mycoplasma hominis infections after neurosurgical intervention. J Neurosurg Pediatr. 2014;14:212-8
41- Mace S E. Acute bacterial meningitis. Emerg Med Clin North Am. 2008;26:281-317, viii.
42-Nau R, Sorgel F, Eiffert H. Penetration of drugs through the blood-cerebrospinal fluid/blood-brain barrier for treatment of central nervous system infections. Clin Microbiol Rev. 2010;23:858-83. 68. Sullins a K and Abdel-

Rahman S M. Pharmacokinetics of antibacterial agents in the CSF of children and adolescents. Paediatr Drugs. 2013;15:93-117

(43)-TERESA CH.,2005:surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. Am J Int Care 2008; 36: 301-308.

(44) Murray P, Ken S.,2005: Medical microbiology. 5 ed: Elsevier Inc.; 2005.

(45)- Klein E, .,2007;Hospitalizations and deaths caused by methicillin-resistant Staphylococcus aureus, United States, 1999- 2005. Emerg Infect Dis 2007; 13: 1840-1846.

(46)-Vincent J-L, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA: the journal of the American Medical Association. 2009; 302(21): 2323-9.

(47)- Nejad SB, Allegranzi B, Syed SB, Ellis B, Pittet D. Health-care-associated infection in Africa: a systematic review. Bulletin of the World Health Organization. 2011; 89(10): 757-65.Navaeifar et al J Pediatr Rev. 2013;1(2) 39 .

(48)-Januel JM, Harbarth S, Allard R, Voirin N, Lepape A, Allaouchiche B, et al. Estimating attributable mortality due to nosocomial infections acquired in intensive care units. Infection Control and Hospital Epidemiology. 2010; 31(4): 388-94.

(49)-.Reunes S, Rombaut V, Vogelaers D, Brusselaers N, Lizy C, Cankurtaran M, et al. Risk factors and mortality for nosocomial bloodstream infections in elderly patients. European journal of internal medicine. 2011; 22(5): e39-e44.

(50)- Foglia EE, Fraser VJ, Elward AM. Effect of Nosocomial Infections Due to Antibiotic- Resistant Organisms on Length of Stay and Mortality in the Pediatric Intensive Care Unit. Infection Control and Hospital Epidemiology. 2007; 28(3): 299-306.