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EMERGING AND RE-EMERGING INFECTIOUS AGENTS OF NOSOCOMIAL DISEASES – THE NEED FOR REVIEW OF HOSPITAL POLICY AND CONTROL STRATEGIES

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ABSTRACT
Nosocomial infections (NIs, now referred to as Healthcare-associated infections, HCAIs) are diseases that essentially originate from the hospital and may be disseminated via biologic or inanimate agents in the healthcare center. They occur globally and constitute major hazards in healthcare institutions resulting in significant morbidity, mortality and increased hospital stay, and high socio-economic cost. Between 3 and 21 percent (average range, 5 – 9%) of all hospitalized patients are affected by HCAIs each year in various communities worldwide; while critically ill, trauma or immunocompromised patients (e.g. those requiring multiple life – saving invasive procedures or immunosuppressive therapy) are hardest hit. The increasing involvement of multiple drug-resistant strains of a large spectrum of emerging and re-emerging infectious agents of NIs complicate morbidity, management and impose serious burden on the patients and relations. Hospital workers, patients, materials or equipments and hospital procedures constitute major factors of transmission mechanism of HCAIs. However, the incidence and socioeconomic impact of NIs (though estimated to be high) are rarely investigated in sub-Saharan Africa (including Nigeria) due to poor healthcare facility and low capacity. There is need for increased awareness on HCAIs and adoption of enduring hospital policy and effective control measures that will take cognizance of emerging trends of nosocomial agents and transmission mechanism to reduce morbidity, mortality and socio-economic impact associated with HCAIs.
Keywords: Healthcare – associated infections, hazards, morbidity, mortality, control measures.

INTRODUCTION

The healthcare environment including medical or oncology wards, surgical operation theaters, intensive care unit (ICU) and the laboratories constitute an important facility in healthcare system. These facilities provide accommodation and special care, succor, segregation and protection for the sick (Pelczar, *et al;* 1993; NNIS, 2001; Gupta, 2012). Personnel and equipment or medical devices also form a necessary and integral part of healthcare institutions (Sonja and Vonberg, 2012). However, such routine and dynamic interactions which occur among both asymptomatic individuals and clinically ill patients, materials and personnel assembled under the same roof frequently enhance the transmission and spread of nosocomial infections (NIs) among patients and hospital workers resulting in significant morbidity and mortality (Hierholzer Jr. and Zervos, 1991; Rubino, 2001; Witherspoon, 2012).

Nosocomial infections (NIs, now commonly referred to as Healthcare-associate infections, HCAIs) are diseases essentially transmitted and acquired by virtue of being present or stay in the hospital, and must not be incubating or present before a patient is admitted into a healthcare center (Garner *et al*; 1988; Odugbemi and Coker, 1988; Saini and Munshi, 2012). They occur worldwide and are regarded as major hazards confronting hospitalized patients and personnel in healthcare institutions globally. Such HCAIs may become clinically apparent, while the patient is still in the hospital or following discharge (Patterson *et al*., 1985; Rubino, 2001).

The Center for Disease Control and Prevention (CDC), estimates that there are about 1.7million cases of HCAIs in the United States (US) alone each year. Of those infections, 99, 000 lead to fatalities. Wenzel (1991) and Mauldin *et al.,* (2010) reported that about 5% of HCAIs occur as part of an epidemic and similar proportions occur as part of a cluster that may spread and cause severe morbidity and mortality in the hospital.

Despite notable advances (i.e. in technology and human capacity development) in the healthcare center sector during the 20th century which revolutionized healthcare delivery in most regions of the world, yet the intractable problems associated with NIs are ever increasing and have become global concern (NNIS, 2001; Giske *et al*., 2008; Shorr, 2009). This development stems from the increasing incidence and severity of NIs involving traditionally recognized agents and evolution of those termed emerging and re-emerging highly virulent infectious agents. The scenario nevertheless, contributes to increased morbidity and mortality in hospitalized patients; burden of discomfort among relatives and high socio-economic cost (Stover *et al*., 2001; Siegel *et al*., 2007; Mauldin *et al.,* 2010). It is believed that excess NIs morbidity and mortality due to treatment failures is estimated to cost over $1 billion dollars per year in North America (Gaynes *et al.,* 1991).

Non-compliance with best hospitals practices and hygiene guidelines by hospital personnel and inability of managers of healthcare institutions (especially in poor-resourced areas including Nigeria) to implement policy on regular and sustained surveillance on NIs and aseptic procedures in hospitals have aggravated the problem of HCAIs (Cabana *et al.,* 1999; Boyce and Pittet, 2002; Larson *et al.,* 2007). The present effort (through review of local and international literature and author's experience in the field) is therefore aimed to highlight the increasing incidence of HCAIs and associated emerging/re-emerging infectious agents including disease burden and complications. It is also aimed to sensitize the stakeholders about the scourge of NIs and proffer measures that will limit their transmission, clinical and socio-economic impact on patients, relations healthcare personnel and community at large.

Epidemiology of Nosocomial Infections

Healthcare-associated infections (HCAIs) have become an increasing problem, with an estimated 2.5million cases reported each year in the United States (US) alone at a colossal cost of about 4.5 billion dollars per annum (Keita – Perse and Gaynes, 1996).

The World Health Organisation (Tikhomirov, 1978) estimates that between 3 to 21 percent (average, 9%) of all hospitalized patients are affected by HCAIs in various communities of the world, while between 5 – 10% of patients admitted to acute care hospitals in North America acquire one or more infections during their stay in healthcare center (Burke, 2003).

In sub-Saharan African, the few available data indicate that nosocomial infection rates (i.e. hospital overall and per service area) range from 2 – 49% (Montefiore *et al.,* 1979; Ojeigbe *et al.,* 1990; Ogunsola *et al.,*1995; Onipede *et al.,* 2004). Studies from various locations showed that significantly high figures of 21.2 – 35.6% of ICU (a very critical unit in the hospital) patients develop an infection during their stay in healthcare facility (Hurr *et al.,* 1999; Burke, 2003). What is more worrisome is the appearance (including emerging and re-emerging agents, Table 1) of multidrug-resistant strains of infectious agents in the hospitals which compound chemotherapy and care resulting in poor prognosis and fatal outcome (Rubino, 2001; Stevens, 2004; Blot *et al.,*2007).

Mortality arising directly from HACIs varies ranging from 0.7 to 2.5%; and 3.4 to 10.9% of HCAIs contributing to deaths in developed countries of the west (Gross *et al.,* 1980; CDC, 1984). However, the figures are believed to be higher in poor-resourced areas of sub-Saharan Africa (Nigeria inclusive) and Asia (as a result of poor healthcare facility, low capacity and poverty) where endemic and epidemic HCAIs are rarely investigated.

Several reports (Gaynes and Horan, 1996; Mims, 1998; Blot *et al.,* 2002; Witherspoon, 2012) have shown that pneumonia is the most common nosocomial infection, followed by urinary tract infections (UTIs) and blood stream infections viz bacteremia or septicaemia (sepsis). Other prevalent infections include surgical wound, and gastrointestinal tract (GIT). On the other hand, although such diseases as nosocomial infective endocarditis (NIE) originating from both native and prosthetic valves appears to be less common, however, it is a well recognized complication especially in critically ill patients who require numerous invasive procedures during treatment. Patients who are mostly affected include those undergoing solid organ transplants (e.g. kidney or liver transplant), endotracheal intubation, indwelling catheterization, burn or wound debridement and skin grafting (Cartotto *et al.,* 1998; Patterson and Dunn, 1999).

Several researchers (Mc Gowon, 1985; Schaberg *et al.,* 1991; Wenzel, 1991; Rubino, 2001; Menon and Menon, 2012) have observed dynamic changes in the spectrum of causative agents of HCAIs involving traditional and those classified as emerging and re-emerging microbial agents (Table 1). For example, increasing occurrences of NIs are now associated with Candida, Aspergillus, Fusarium and Trichosporon species among Fungi (Anderson, 1991; Menon and Menon, 2012). Among viral agents, respiratory Syncytial virus, Rota virus, Influenza virus and Hepatitis C virus are increasingly involved in HCAIs (Breuer and Jefferies, 1990; Rubino, 2001). However, majority of HCAIs reported were still associated with bacterial agents (Hierholzer and Zervos, 1991; Witherspoon, 2012).

Sources and Reservoir of Nosocomial Infections

Infections in the hospital setting can be acquired either through endogenous or exogenous sources. In many cases, endogenous infections result from patients own flora which, at the time of infection, may invade patient's tissues spontaneously. Such autoinfection may occur through transfer of infectious agents from one anatomic site to another e.g. nose or skin to wound or may be released from, for example, bowel via anal region to urinary tract e.g. *Escherichia coli.* Infections may also be introduced into tissues by surgical operation, nursing procedures and instrumental manipulation including indwelling devices such as central lines, endotracheal tubes and catheters. The various catheters used that may harbor microorganisms include central venous catheters including urinary, intravascular and haemodialysis catheters (Pelczar *et al.,* 1993; Mims *et al.,* 1998). On the other hand, other sources of infections in healthcare institutions include infected or clinically ill and asymptomatic persons (i.e. patients, hospital staff viz Doctors, Nurses, Laboratory Personnel etc and patient's relations).

Arthropod vectors (e.g. Anopheles Mosquitoes) may also serve as transmitters or carrier of infections in the hospital.

Table 1: Traditional, Emerging and Re – Emerging Infectious Agents Associated with Nosocomial Infections.

Infectious Agents/Classification:

Category of Organism	Traditional	Emerging	Re – emerging
Bacteria	*Streptococcus pneumoniae,* Coagulase negative Staphylococcus sp. Group D Streptococcis/Enterococcus sp. Salmonella sp., Proteus sp. *Staphylococcus aureus, Escherichia coli, Acinetobacter sp., Klebsiella sp. X. maltophila, P. aeruginosa* Shigella sp., Serratia sp., *S. marcenscens, Bacteroides* sp and other *anaerobes.*	MRSA* *A. baumannii** *Burkholderia cepacia** *Corynebacterium amycolatum* *Ralstonia picketti* *Citrobacter diversus* *Legionella pneumophila* *Campylobacter sp.* *Strenotrophomonas maltophila* VRSA* *Clostridium difficile**	*M. tuberculosis**, *Bordetella sp.,* *Acinetobacter sp**. *Enterococcus sp**. *VRSA**
Viruses	Hepatitis A virus, Rota virus, Adenovirus Norwalk virus Calci virus Enteroviruses	HIV, SARS, Lassa fever virus (Arena virus) Ebola virus Human T – cell lymphocytic Virus (HTLV) Papilloma virus, Korean hemorrhagic fever virus (Hanta/Bunya virus)	Hepatitis B and C viruses, Measles viruses, Varicella zoster virus Influenza virus, Mumps virus, Respiratory syncyitial virus (RSV), Human cytomegalo virus (CMV),
Fungi	*Candida albicans+* Aspergillus sp.	Malassezia sp. Trichosporon sp. Fusarium sp. *C. albicans* Acremonium sp.	*C.albicans* Aspergillus sp. Acremonium sp.
Parasites	*Plasmodium* sp. (Malaria) *S. scabii*		

(Graham *et al.*, 1981; NFID, 1999; Knox and Holmes, 2002; Siegel *et al.*, 2007; Weber *et al.*, 2010;Menon and Menon, 2012)
MRSA – Methicillin – resistant *S. aureus*, HIV – Human Immunodeficiency Virus,
VRSA – vancomycin – resistant *S. aureus,* ** – Resistant to multiple antibiotics*

The environmental sources of infections often implicated in NIs include medical devices/equipment (e.g. surgical instruments, dialysis equipment, endoscope, suction machine, etc), fixed devices (e.g. air conditioner, humidifiers, etc) that are installed in the hospital for use. Others are medical solutions (including infusates or intravenous solutions), food items and water which are contaminated with pathogens and are ingested while in the hospital. Respiratory secretions resulting in short distance acquisition of infectious agents or 'droplet nuclei' may lead to respiratory nosocomial diseases. Blood and blood products (especially in blood transfusion) and solid organ for transplant have severally served as sources of severe HCAIs (Patterson *et al.,* 1985; Hierholzer Jr. and Zervos, 1991; Gaynes and Horan, 1996). Infectious agents from these sources or reservoirs may be acquired via direct or indirect contact with such origins.

Mechanism of Transmission of Nosocomial Infections

There are various ways in which HCAIs are transmitted from a source or reservoir of infectious agent to a susceptible host. Some of the widely recognized modes of transmission include by direct contact with infected patients, hospital personnel or asymptomatic carriers (Hierholzer Jr. and Zervos, 1991). Other routes that are commonly implicated in disease transmission in the hospital environment include air-borne dissemination from respiratory secretion or 'droplet nuclei' and aerosols produced by equipment such as nebulizers, humidifiers and air conditioners.

Many patients and hospital workers have contracted infections in the hospital via ingestion of contaminated food items, water and other fluids including some medications such as syrups and other pediatrics suspensions.

Parenteral inoculation via contaminated needles and syringes, surgical instruments, intravenous fluids and blood transfusion is well acknowledged in the health care institutions globally (Mims *et al.*, 1998; Agul, 2001). Similarly, overcrowding, poor ventilation and exposure to insect vectors (e.g. Mosquito bites) predispose patients, workers and visitors to infection (Pelczar *et al.*, 1993). Contact with contaminated utensils, hospital devices or equipment also serve as common mode of disease transmission (Gaynes and Horan, 1996; Witherspoon, 2012).

Risk Factors of Healthcare Associated Infections

Hospitals are centres where both infected patients (who harbor and are potential sources of infections) and susceptible or vulnerable subjects (who are potential recipients) are accommodated. These include hospitalized patients, healthcare personnel, visitors alike and patients' relatives (Agul, 2001). Generally, hospitalized patients have an increased susceptibility to infections due to various reasons arising from their underlying clinical conditions. Factors that may enhance the possibility of infectious disease transmission and acquisition in hospitals include length of hospital stay (e.g. > 8.4 days increase risk) and overcrowding (Stevens, 2004). Host related factors that may increase susceptibility to infections include general health status, extreme ages (e.g. young – i.e. neonates, infants and the elderly are more susceptible to infections), pregnancy, neutropenia, chronic illnesses or debilitating diseases (e.g. cancers, cardiovascular, hepatic or renal failure, hemophilia, and diabetes mellitus), and immunosuppression (e.g. HIV infection, steroid therapy and cancer treatments) (Pelczar, 1993; Keita – Perse and Gaynes, 1996; Agul, 2001; Mauldin *et al.*, 2010). Hospital invasive procedures for diagnostic purposes and treatment also put patients at greater risk of infections. These include bone marrow and solid organs transplants, haemodialysis, blood transfusion, surgery, endoscopy, laparoscopy, local therapy for burns and wounds as well as implantation of indwelling catheters (Hurr *et al.*, 1999; Burke, 2003; Siegel *et al.*, 2007). These factors either compromise the immunity of the patients or cause defects in the intrinsic barriers to microbial invasion and thus increase susceptibility to microbial invasion.

Hospitals practices such as level of observation of aseptic procedures (e.g. sterilization and disinfection of hospital items including regular hand washing between contact with patients and thereafter), quality of hospital manpower and administrative policies via level of awareness, policy adherence and implementation by hospital personnel and quality of hospital management play a significant role in the rates of occurrence of hospital – acquired infections in health institutions (Cabana *et al.*, 1999; Rubino, 2001; Boyce and Pittet, 2002; Larson *et al.*, 2007).

Useful Control Strategies for Healthcare Associated Infections

In view of the challenges posed by increasing incidence of NIs and emergence of highly virulent and drug – resistant associated infectious agents often spread by various routes or mechanisms in healthcare centers, there is need to adopt a holistic approach in the control of HCAIs. Some useful measures to achieve this goal are outlined in table 2. If adopted according to specific need of the health institution, it will go a long way in checking the increasing rates of HCAIs at all levels of healthcare system.

Table 2a: Preventive and Control Measures for Hospital – Acquired Infections

Preventive/control measures can be achieved by taking the following measures:

- Blocking transmission of infectious agents and nosocomial spread and reduce unavoidable exposures to infections.
  - Strict implementation and observance of aseptic procedures in all hospital practices and techniques including adequate disinfection/sterilization of hospital items prepared for use on patients.
  - Clean linens should be used in all hospital wards and each bed should be washed and disinfected after each discharge.
  - Individual hygiene practices with hand – washing (e.g. washing of hands before and after contact with the patient) being the most cost effective should be encouraged.
  - Environmental hygiene involving cleaning and disinfecting of contaminated surfaces should be strictly effected. The use of chlorine derivatives is efficient, cost effective and easily accessible. Alternatively, Glutaraldehyde, Iodine, derivatives, and, to a lesser extent alcohols and detergents may be used.
  - Mandatory use of physical barriers for individual protection, such as disposable gloves, gowns, glasses, masks and occlusive dressing for hand and face injuries should be enforced.
  - Biological specimens and contaminated medical equipment must be handled according to standard precautions. Adapted safety packaging should be used for transporting biological samples.
  - Proper waste management should be accorded priority for the overall hygiene and safety of the hospital environment.

Table 2b: Preventive and Control Measures for Hospital – Acquired Infections

Preventive/control measures can be achieved by taking the following measures:

- Infection sources, transmission, acquisition, and the spread can be controlled by specific practices including;
  - Protective isolation of highly susceptible patients to pathogens (e.g. in organ transplant) is highly encouraged.
  - Infected hospital personnel should be excused from duty and from performing his/her routine activities until after treatment is achieved.
  - Susceptible individuals can be given prophylaxis against certain infections (e.g. RSV, VZV and HBV) and thus boosting specific immunity of patients and reducing risk factors e.g. neutropenic or immunosuppressed patients or those on cytotoxic therapy.
  - Infected persons should be excluded from donating blood or organs.
  - Rational and judicial use of prophylactic and therapeutic antibiotics should be enforced by good administration policy to minimize resistance.
  - Good ventilation should be provided and overcrowding avoided.
  - Patients' visitors and workers should be protected against insect bites. (e.g. Mosquito bites) by using physical barriers (e.g. Insecticide – treated bed nets, window/door nets) and insecticide spray to limit exposure to parasitic/protozoan infections like malaria.
  - Hospitals should setup infection control programmes/committee with regular surveillance of endemic and epidemic NIs outbreak.
  - Effective and proactive hospital administration is imperative for successful implementation of infection control.
  - Maintenance of record so as to monitor the efficacy of the system should be encouraged.

(Cabana *et al.,* 1999; Hurr *et al.,* 1999; Rubino, 2001; Stevens, 2004; Siegel *et al.,* 2007; Sherwal and Rakshit, 2012)

CONCLUSION

Infection control interventions have been proved to significantly reduce the incidence (both endemic and epidemic) of NIs and exhibit a high – cost benefit ratio. Nosocomial infections now require greater attention in healthcare setting because of increasing associated morbidity, mortality and high – socio economic cost. Both traditional and emerging or re – emerging infectious agents of NIs have important infection control implications that must be given adequate considerations in hospital protocols and guidelines that will aid their recognition, isolation/identification and accurate diagnosis. The uses of molecular epidemiological analyses are the current techniques for reliable diagnosis of infectious diseases. This is because, in most cases, they are prompt, definitive and conclusive. Although new control strategies should continuously be developed according to need, however, it should be recognized that aseptic procedures and observance of good personal and environmental hygiene will continue to form the bedrock and fundamental component of any control measures aimed at limiting HCAIs in a long time to come.

RECOMMENDATIONS

Hospital workers need regular update so as to improve their understanding and recognition of mechanism of transmission and spread of NIs for effective preventive measures. The approaches to prevention and control of HCAIs need to be tailored to the specific needs and peculiarity of each component unit of the healthcare center.

Molecular epidemiology is the gold standard currently used in the investigation of HCAIs; but the technique is rarely used in most developing world of sub-Saharan Africa due to inadequate facility and man power. However, appropriate methods must be adopted to determine the epidemiologic markers of NIs and must be modified for each organism group under investigation. It is imperative that the administration of healthcare institutions needs to ensure that appropriate policy is introduced, strategies are fully implemented, regularly evaluated for effectiveness and such that there is significantly reduced incidence of NIs in their centers. For example, a multidisciplinary process or committee should be setup to monitor and improve hospital care practices, adherence to recommended practices for standard aseptic and contact precautions, and also monitor NIs in its centre.

It must be reiterated that successful prevention and control of HCAIs require administrative, scientific, technical, and professional leadership. It also requires a financial and adequately trained human resource commitment for any meaningful impact. Therefore these resources must be made available for any meaningful implementation of infection control and preventive measures can be achieved in the healthcare centers at all levels.

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