

Research Article

Contemplating Catheter Induced Blood Stream Infections and Associated Risk Factors in Diverse Clinical Settings: A Comprehensive Review

Zahra Zahid Piracha¹, Sadia Mansha², Amna Naeem³, Umar Saeed^{4*}, Muhammad Nouman Tariq⁵, Azka Sohail⁶, Kashfia Hassan⁷, Muhammad Waseem⁸, Muhammad Shahmeer Fida Rana⁵, Syed Shayan Gilani⁵, Seneen Noor¹ and Elyeen Noor¹

¹International Center of Medical Sciences Research (ICMSR), Islamabad (44000), Pakistan

²Punjab Medical College, Faisalabad, Pakistan

³Quaid e Azam University, Islamabad, Pakistan

⁴Clinical and Biomedical Research Center (CBRC) and Multidisciplinary Laboratories (MDL), Foundation University School of Health Sciences (FUSH), Foundation University Islamabad (FUI), Islamabad (44000), Pakistan

⁵Akhtar Saeed Medical & Dental College (AMDC), Lahore, Pakistan

⁶Central Park Teaching Hospital, Lahore, Pakistan

⁷Islamabad Medical and Dental College, Islamabad, Pakistan

⁸Alkhidmat Raazi Hospital, Rawalpindi, Pakistan

More Information

*Address for Correspondence:

Dr. Umar Saeed, Clinical and Biomedical Research Center (CBRC) and Multidisciplinary Laboratories (MDL), Foundation University School of Health Sciences (FUSH), Foundation University Islamabad (FUI), Islamabad (44000), Pakistan, Email: umarsaeed15@yahoo.com

Submitted: October 17, 2023

Approved: November 01, 2023

Published: November 02, 2023

How to cite this article: Piracha ZZ, Mansha S, Naeem A, Saeed U, Tariq MN, et al. Contemplating Catheter Induced Blood Stream Infections and Associated Risk Factors in Diverse Clinical Settings: A Comprehensive Review. *J Clin Intensive Care Med.* 2023; 8: 014-023.

DOI: 10.29328/journal.jcicm.1001044

Copyright License: © 2023 Piracha ZZ, et al.

This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Keywords: Catheter; Bloodstream infections; Sepsis; Bacteremia



Abstract

Catheter-Related Bloodstream Infections (CRBSIs) are severe healthcare-associated complication that occurs when bacteria enter the bloodstream through a catheter. The risk of CRBSIs is influenced by various factors. Prolonged catheter placement increases the risk, as each day increases the potential for bacterial colonization and bloodstream infection. Proper aseptic technique and a sterile environment during catheter insertion are essential to minimize infection risk. Stringent infection control measures during insertion, including sterile gloves, thorough hand hygiene, and appropriate skin disinfection, are crucial. Inadequate catheter site care and suboptimal catheter management can contribute to CRBSIs. Regular cleaning, disinfection, and dressing changes are necessary to reduce the risk of infection. The type of catheter used also affects infection risk. Central Venous Catheters (CVCs) and arterial catheters, especially those inserted into the jugular or subclavian vein, carry a higher risk of CRBSIs compared to peripheral venous catheters. Individuals with compromised immune systems, such as chemotherapy patients, organ transplant recipients, and those with HIV/AIDS, are more susceptible to CRBSIs. Patients with existing infections, like pneumonia or urinary tract infections, are at a heightened risk of acquiring CRBSIs due to potential cross-contamination. Healthcare professionals who fail to practice thorough hand hygiene before and after catheter-related procedures can introduce pathogens into the bloodstream. Leaving catheters in place when no longer necessary or using them unnecessarily elevates the risk of infection. To prevent CRBSIs, strict infection control protocols, including effective hand hygiene, sterile catheter insertion techniques, routine site care, and prompt catheter removal when no longer needed, are imperative. Healthcare facilities often implement specific protocols to mitigate CRBSI risk and enhance patient safety.

Introduction

Sepsis or bacteremia, can happen due to different variables. Common hazard components related to circulatory system contaminations may cause sepsis. With intrusive therapeutic approaches that involve the installation of therapeutic devices or access to the circulatory system, the risk of circulatory system infection increases. This includes the use of surgical techniques, mechanical breathing, urine catheters, blood

vessel catheters, and central venous catheters. The next risk factor for circulatory system disorders is in people with compromised resistant frameworks. This includes those with HIV/AIDS, cancer patients receiving chemotherapy, recipients of organ transplants, and people with specific immune system disorders. People at both ends of the age spectrum, such as babies and the elderly, are more likely to have circulatory system infections. Although the elderly usually have impaired safe responses, newborns have adolescent-like safe systems.



Patients with persistent illnesses, such as diabetes, renal disease, liver disease, or lung infection, are more likely to develop circulatory system disorders as a result of the effects of these ailments on the immune system. The susceptibility to circulatory system contaminations is increased by factors that weaken the secure system, such as long-term use of immunosuppressive drugs, corticosteroids, or specific cancer medications. Patients who are hospitalised are more likely to get circulatory system infections, especially if they need interventional procedures, have surgical wounds, or are in intensive care units. Circulatory system infections can be brought on by healthcare-related infections, such as those acquired during hospital stays.

Later diseases

Having an existing disease, such as pneumonia, urinary tract disease, or skin and delicate tissue disease, increases the chance of creating a circulatory system disease in the event that the contamination spreads to the circulatory system. Lack of hand hygiene on the part of healthcare professionals, patients, or visitors might encourage the spread of germs and raise the risk of contaminating the circulatory system. Using indwelling devices, such as intravascular catheters, ventilator-associated devices, or urine catheters, can introduce pathogens into the circulatory system and cause disease. The emergence of microbes that are resistant to antibiotics makes it more difficult to treat infections of the circulatory system and raises the risk of consequences. It is important to remember that risk factors might change based on the person, the type of defilement, and the healthcare environment. Circulatory system contaminations can be prevented by taking preventive actions including maintaining extreme cleanliness, putting disease control customs into practice, and using antimicrobials wisely [1-7].

Risk factors involved in disease aggravation

In order to discover risk factors for bloodstream infections among patients at a hemodialysis centre in Brazil, Dayana Farm and associates carried out a case study in 2015. On patient data collected, they used logistic regression to accomplish their goal. In comparison to patients who had an arteriovenous fistula for vascular access, the data showed that patients with central venous catheters had an 11.2-fold higher likelihood (with a 95% confidence interval of 5.17 - 24.29) of getting bloodstream infections. Further, with a 95% confidence interval of 1.9 - 23.09, previous hospitalisation increased the risk of bloodstream infections by 6.6-fold. Variables like hypertension, prior peritoneal dialysis therapy, the kind and timing of the current venous access, the type of the prior venous access, and previous peritoneal dialysis were all included in the initial logistic regression analysis [8].

Despite the fact that Bloodstream Infections (BSIs) in patients with the human immunodeficiency virus (PWH) cause significant morbidity and mortality, the background of

this study demonstrates the dearth of knowledge surrounding these illnesses. The authors sought to investigate the epidemiology, microbiology, and clinical results of PWH-related community- and hospital-acquired BSI. The study identified all BSI cases in PWH at Southern Alberta Clinic using information from laboratory and clinical databases between January 1, 2000, and December 31, 2017. The authors utilised Cox proportional hazards models to examine risk factors connected to BSI and derived crude incidence rates for BSI and death per 1000 person-years. A 1-year death rate following BSI was studied using logistic regression models with generalised estimating equations. The findings revealed that 396 episodes of BSI were encountered by 8% (228) of the 2895 PWH. Gram-positive bacteria made up 72% of BSI cases, whereas Gram-negative bacteria made up 28% of them. The most vulnerable PWH to BSI had lower CD4 nadirs, higher Charlson comorbidity indices, and hepatitis C virus. A higher risk of long-term all-cause death was also linked to BSI. Polymicrobial BSI (19%) and repeat episodes (42%) were both frequent. According to the study's findings, BSI in PWH still poses a serious threat because of its high recurrence incidence, associated morbidity, and mortality. The study's conclusions can be used to pinpoint PWH who are most at risk for BSI, which will help in the development of focused therapies. The research highlights PWH with low immunity [9].

Childhood malnutrition and bloodstream infection

Childhood malnutrition is a global issue that has a significant impact on morbidity and mortality in children. Malnutrition and infection have a synergistic effect, making children more susceptible to infections caused by viruses, bacteria, protozoa, and helminths. The inadequate intake of protein and calories, combined with micronutrient deficiencies, is the most common cause of childhood malnutrition. The factors that lead to impaired host defense in these children are not well-defined. This review examines the literature related to impaired host defense and the risk of infection in primary childhood malnutrition, with particular attention to longitudinal and prospective cohort human studies and studies of experimental animal models that investigate causal, mechanistic relationships between malnutrition and host defense. Protein and micronutrient deficiencies affect the hematopoietic and lymphoid organs, compromising both innate and adaptive immune functions. Malnutrition-related changes in intestinal microbiota contribute to growth faltering, dysregulated inflammation, and immune function. While there has been progress in understanding the synergistic effects of malnutrition and infection, there are still critical gaps in our knowledge. Further mechanistic studies are necessary to identify targeted interventions that can improve host defense and reduce morbidity and mortality in this vulnerable population [10].

The Infectious Diseases Society of America (IDSA) advises



treating CRBSI disease with antibiotics for 7 days – 14 days. Between January 2010 and October 2016, a retrospective phase 1 investigation was carried out to review the microbial epidemiology, as well as to ascertain the frequency of relapse and the risk factors connected to it. In phase 2, patients without relapse risk factors were prospectively enrolled to undergo antibiotic therapy for 7 days following catheter removal, and their outcomes were compared to those of a control group that underwent antibiotic medication for about 14 days. The most frequent infections discovered in CRBSI cases, according to the study, were *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Stenotrophomonas maltophilia*. Catheter retention was the only risk factor significantly linked to relapse, with a relapse rate of 6.4%. In phase 2, relapse rates were reduced with short-duration therapy compared to long-duration therapy. According to the study's findings, empiric broad-spectrum antibiotic therapy with sufficient *P. aeruginosa* coverage should be used to treat simple GNB CRBSI. Relapse prevention requires catheter removal, and treatment duration reduction may be an option. The study emphasises how crucial it is to tailor the length of antibiotic therapy in order to enhance patient outcomes and lower the danger of antibiotic resistance [11].

Obesity and bloodstream infections

Primary prevention should be a top priority since Bloodstream Infections (BSI) are a significant source of morbidity and mortality. The purpose of this study was to look into the relationship between lifestyle choices and BSI risk. With a median follow-up of 14.8 years, the study included a prospective cohort study of 64,027 people from the Norwegian HUNT2 Survey. The findings showed that compared to participants who were of normal weight, those who were overweight or obese had a greater risk of BSI and BSI mortality. Physically inactive participants had a considerably higher risk of BSI and BSI mortality compared to the most physically active, while current smokers had a significantly higher risk of BSI and BSI mortality than never-smokers. These findings imply that obesity, smoking, and inactivity may all be changed [12].

Data from 387,109 men and women living in England were evaluated as part of the UK Biobank investigation. Physical inactivity, smoking, alcohol consumption, and obesity were evaluated as lifestyle factors, and they were analysed using questionnaires and body mass index measurements. Interest was focused on the 760 COVID-19 cases that required hospital admission between 16 March 2020 and 26 April 2020. The study discovered that heavy drinking did not raise the likelihood of COVID-19 hospital admission, but obesity, smoking, and inactivity did. The study also demonstrated that participants in the category with the worst lifestyle scores had a 4-fold higher chance of developing COVID-19 than those in the category with the best lifestyle scores. Additionally, high levels of C-reactive protein were linked to an increased risk of

COVID-19, which helped to explain the links between a poor lifestyle and the disease. According to the study, unhealthy habits could together account for up to 51% of the population's attributable proportion of severe COVID-19. The study comes to the conclusion that making little adjustments to one's lifestyle can reduce the risk of developing serious infections and that living an unhealthy lifestyle that increases the risk of non-communicable diseases also increases the likelihood of contracting COVID-19 and requiring hospitalisation, presumably as a result of low-grade inflammation [13].

Home parenteral nutrition and bloodstream infections

Patients who receive Home Parenteral Nutrition (HPN) face a serious risk of developing Catheter-Related Bloodstream Infections (CRBSI). 18 kids and 125 adults participated in a study to find the CRBSI risk factors. All patients who received HPN injected at least twice weekly for at least two years between January 1, 2006, and December 31, 2011, were included in the study. The study examined medical records from a national home care pharmacy. Data on risk factors and infections were gathered throughout this time. The use of multiple lumen catheters, subcutaneous infusion ports rather than tunnelled catheters, higher frequency of lipid emulsion infusion, drawing blood from the CVC, and infusion of non-PN drugs via the CVC were all found to be significant risk factors for CRBSI in adults, according to the findings. In children, but not in adults, an increase in PN frequency was linked to an increase in the risk of CRBSI. Additionally, povidone-iodine disinfection of catheters was more successful than isopropyl alcohol alone. The study identified multiple CRBSI risk variables that are already treatable with straightforward interventions. To assess the efficacy of regimens incorporating chlorhexidine, additional research is required [14].

For patients receiving Home Parenteral Nutrition (HPN), preventing Catheter-Related Bloodstream Infection (CRBSI) is essential because it is a significant consequence. In order to lower the incidence of CRBSI in high-risk patients, Ethanol Lock Therapy (ELT) and Antibiotic Lock Therapy (ALT) have been suggested as preventative strategies. The authors of this study sought to estimate the overall number of infections in all eligible patients participating in the Mayo Clinic HPN programme between January 1, 2006, and December 31, 2013, both before and after ALT or ELT. 313 CRBSI episodes were experienced by the 63 patients who were enrolled in the trial overall. 49 of these took place after locking while 264 occurred prior. When compared to before locking, the infection rate per 1000 catheter days was significantly lower after locking. According to the findings, ALT or ELT can be useful in lowering the overall rate of infections in patients receiving HPN and should be taken into consideration in the right therapeutic conditions [15].

72 adult patients with intestinal failure who received HPN at a single referral facility in Bangkok between October 2002 and April 2014 were included in the study. There were 21



CRBSIs in 10 individuals over a 12-year period, resulting in a CRBSI incidence of 1.47 per 1000 catheter days. A higher prevalence of CRBSIs was linked to the use of implanted ports, alcohol-based povidone-iodine solution as a disinfectant, cyclic HPN infusion, hospital-based compound HPN formulations, and longer duration of HPN. Longer lengths of HPN, cyclic HPN, and compound HPN seen in hospitals were all significant predictors of CRBSIs, according to multivariate analysis. The results indicate that to reduce HPN-related problems and prevent CRBSIs, individualised therapy with a multidisciplinary team in centres with competence in HPN management is required. The key to reducing CRBSIs in patients receiving long-term HPN is strict adherence to evidence-based instructions by patients and carers, as well as appropriate supervision by well-trained HPN providers [15].

Although the global burden of infection is still high, effective public health measures like handwashing and vaccinations are important in reducing the spread and impact of infections. Acute respiratory tract infections alone were to blame for 2.38 million fatalities worldwide in 2016. A wealth of mechanistic and clinical data highlighting the significance of micronutrients and omega-3 fatty acids, including vitamins A, B6, B12, C, D, and E, folate, zinc, iron, selenium, magnesium, copper, and Eicosapentaenoic Acid (EPA), and Docosahexaenoic Acid (DHA), in supporting optimal immune function, confirm the critical role of nutrition in supporting the immune system. Although it happens frequently, inadequate intake and status of these nutrients reduces resistance to infections and increases disease burden. Therefore, it is crucial to think about nutritional supplementation as a secure, efficient, and affordable method to support ideal immune function. For particular nutrients, such as vitamins C and D, supplementation with micronutrients and omega-3 fatty acids over the Recommended Dietary Allowance (RDA) but within the advised upper safety limits is justified. Public health professionals are urged to include dietary measures in their suggestions for enhancing public health [16].

The data were acquired retrospectively from a Boston Home Infusion company that, between 2005 and 2011, administered HPN therapy to 212 patients with GI-related illnesses and oncology. The findings revealed that 25 catheter problems affected 11.7% of the 163 patients, at a rate of 1.30 per 1000 Peripherally Inserted Central Catheter (PICC)-line days. In comparison to patients with oncology-related illnesses, those with catheter difficulties had more PICC-line days, more hospital admissions, and an ICD-9 diagnosis for GI-related disorders. The study's drawbacks include its retrospective methodology and reliance on data from a single centre. Despite the fact that it offers some helpful insights into catheter problems related to HPN therapy, the study has some important limitations. Further study is therefore required to explore potential risk factors for catheter complications in patients receiving HPN therapy and to validate these findings [17].

Central Line-Associated Bloodstream Infection (CLABSI) is a significant complication that can be life-threatening in the context of Home Parenteral Nutrition (HPN). Potential indicators of CLABSI in adult HPN patients were looked into in this study. To gather demographic and clinical information, the medical records of 114 patients treated by the Hospital of the University of Pennsylvania's HPN programme between January 1, 2018, and June 30, 2019, were examined. Experts in infectious diseases proactively made decisions regarding CLABSIs. Potential predictors of CLABSI were found using logistic regression models. It was discovered that there were 0.89 CLABSI cases for every 1000 catheter days. In one multivariate model, ostomy/wound, tunneled/implanted catheter, and BMI 18.5 were found to be predictors of CLABSI. Patients with two potential predictors and a tunneled or implanted catheter were discovered to be at a high risk of CLABSI in a second model. The study emphasises the significance of appropriate wound and catheter management, particularly in patients with multiple predictors, and the utilisation of several catheter types to lower CLABSI rates. Rapid malnutrition treatment may also help lower the risk of CLABSI, though further studies are required to prove this [18].

Bloodstream infections among cancer patients

Due to their immunocompromised state, cancer patients who receive Home Parenteral Nutrition (HPN) are more likely to acquire CRBSI. The frequency of and risk variables for CRBSI in cancer patients having HPN treated using a standardised catheter care routine were assessed in this retrospective cohort analysis by the authors. With the incidence of CRBSI represented as occurrences per 1000 HPN days as the primary outcome, the study comprised 335 cancer patients receiving HPN between January 2012 and July 2015. The Venous Access Devices (VADs) employed were either subcutaneous implanted ports, Tunneled Central Catheters (TCCs), or Peripherally Inserted Central Catheters (PICCs). The variables connected to CRBSIs were identified by the authors using univariate Poisson regression analyses. According to the study's findings, a standardised catheter maintenance procedure in a high-risk oncology group receiving HPN resulted in a low rate of CRBSI (0.54 per 1000 HPN days). 50.5% of the 408 VADs under study had ports, 46.8% had PICCs, and 2.7% had TCCs. There were 16 CRBSI incidents in total, with colorectal, pancreatic, ovarian, and stomach cancers being the most prevalent. No factors were discovered to be statistically significantly linked with the prevalence of CRBSI after univariate analysis. Overall, the study indicates that high-risk oncology patients receiving HPN may experience CRBSI less frequently with the use of a routine catheter care approach. However, more research is required to ascertain the efficacy of this strategy in other patient populations and to pinpoint additional CRBSI risk factors [19].

Hemodialysis and bloodstream infections

To determine risk factors for Catheter-Related



Bloodstream Infections (CRBSI) in patients receiving non-tunneled hemodialysis and having either acute kidney injury or chronic kidney disease, the study revealed that 12.6% of 111 individuals who underwent retrospective examination experienced CRBSI. Three independent predictors of the development of CRBSI were found: the mean platelet volume, the admission serum albumin level, and the length of the catheter. The study also showed that the existence of CRBSI was predicted by a catheter stay of 22 days. The retrospective form of the study restricts the ability to establish causality, despite the fact that it offers helpful insights into the determinants of CRBSI in a particular patient population. Furthermore, the results of the study might not apply to other patient groups, particularly those with different comorbidities or undergoing various forms of renal replacement therapy. In order to confirm the results of the present investigation and establish additional possible predictors of CRBSI in patients with acute renal injury or chronic kidney disease receiving hemodialysis, additional studies, especially those with a prospective design, are necessary [20].

For hemodialysis, Tunnelled Cuffed Catheters (TCCs) are frequently used until permanent arteriovenous access is established. TCC use, however, may result in side effects including infections, catheter malposition or dysfunction, or venous stenosis. Despite this, little is known about the long-term effects and problems of TCC use in our nation. The purpose of this study was to look into the effects and long-term problems related to TCC use. For patients who got TCCs for hemodialysis at our facility between January 2016 and June 2018, a retrospective study of patient files was done. During the study period, 116 TCCs were implanted, with a mean patient age of 57.09 years and 58.6% of cases involving males. The right internal jugular vein (52.6%) and the left internal jugular vein (29.3%) were the two sites where TCCs were most frequently inserted. Once permanent access was mature, functioning TCCs were successfully eliminated in 65.7% of instances. 19.8% of patients experienced Catheter-Related Bloodstream Infections (CRBSI), which required catheter removal in 12.6% of cases. In 6.3% of patients, mechanical issues requiring catheter removal were observed. Between 1 and 343 days, the median catheter stay lasted 62.5 days. This study demonstrates that TCCs can be a viable choice for short- to intermediate-term hemodialysis use until permanent arteriovenous access can be provided in resource-constrained situations, despite the fact that they have significant drawbacks, namely CRBSI [21].

It is well recognised that using non-tunneled catheters for hemodialysis is linked to a high prevalence of problems, such as infections and thrombosis. In this cross-sectional investigation, the authors sought to ascertain how frequently catheter infections occurred in hemodialysis patients in a Tertiary Care Hospital in Karachi despite the use of antibiotic locks. Bloodstream infections caused by catheters were discovered in a total of 21 out of 120 patients (17.5%), with

coagulase-negative Staphylococci and vancomycin-resistant Enterococcus being the most typical pathogens observed. The high incidence of infections shows that non-tunneled catheters should only be used with caution in hemodialysis patients, even if gentamicin lock solution appears to be effective against gram-negative infections. It is necessary to conduct more studies to examine other methods for protecting this population against catheter-related infections [22].

Nutritional therapy and bloodstream infections

In adolescents with eating disorders receiving nutritional therapy via a Peripherally Inserted Central Catheter (PICC), this study sought to identify the risk factors for Catheter-Related Bloodstream Infection (CRBSI). Although CRBSI is a frequent side effect of central venous hyperalimentation, the causes of its occurrence in people with eating disorders are unknown. From January 2012 to December 2019, 51 patients who received nutritional therapy with PICC underwent a retrospective review. White Blood Cell (WBC) count and weight trends were analysed, and CRBSI onset variables were identified. Also presented was a case series of CRBSI brought on by *Candida parapsilosis*. The study discovered that in eating disorder patients getting nutritional therapy using PICC, persistent resistance to weight gain was a risk factor for developing CRBSI. In the majority of patients, the minimal weight day occurred on or before day 7, and it was preceded by the day with the lowest WBC count. When compared to patients who did not develop CRBSI, those who did experienced a significant delay in the minimum weight day. The median WBC count preceding CRBSI in the case series of *C. parapsilosis*-related CRBSI fell to 2,570/L at a median of day 36, and CRBSI manifested at a median of day 38. The immediate removal of the PICC and administration of an antifungal medication led to a full recovery in all patients without any side effects. According to the study, there is a risk of developing CRBSI in patients with eating disorders undergoing nutritional therapy through PICC, even with increased appetite and weight gain, constant monitoring of WBC count is advised [23].

Extensively resistant *acinetobacter baumannii* among neonates

An insightful examination into a bloodstream infection outbreak among newborns brought on by a very resistant strain of *Acinetobacter baumannii* is presented by Ulu-Kilic and colleagues. The concentrated methodology and in-depth examination of this specific bacterial strain by the authors provide a thorough knowledge of the grave implications for newborn health. According to the study, the worrisome resistance of the bacterial strain to various treatments highlights the urgent need for continued observation and the creation of novel medicines or therapeutic modalities. The detailed documentation of the outbreak, its management, and subsequent recommendations contribute valuable information for future prevention and control strategies.



Despite the study's specific focus on a single outbreak, the insights generated have far-reaching implications for understanding and managing similar infections. However, its applicability to broader contexts may be limited due to the specific population (neonates) and the bacterial strain studied. Despite this, the study stands as a critical reminder of the challenges in managing catheter-induced bloodstream infections, especially those caused by multi-drug resistant organisms, and underscores the importance of swift, effective responses to outbreak situations in neonatal healthcare settings [24].

Candida catheter-related bloodstream infection

The safety and survival of patients receiving Home Parenteral Nutrition (HPN) are seriously endangered by Catheter-Related Bloodstream Infections (CRBSIs). To maximise the efficiency of HPN programmes, this study analyses the incidence, species distribution, risk factors, outcomes, and therapeutic approaches for *Candida* CRBSIs in HPN patients. 20 papers total—six paediatric and 14 adult—were included in the study. 9.8% of paediatric and 11.7% of adult CRBSIs were caused by *Candida*. *Candida albicans* and *C. parapsilosis* were the most common *Candida* species producing CRBSIs in paediatric patients, whereas *C. albicans*, *C. glabrata*, and *C. parapsilosis* were most common in adult patients. Risk factors for child HPN CRBSIs include prior fungaemia and underlying haematological conditions. About 30% of deaths were attributed to candida infections. According to current recommendations, catheters should be removed before starting systemic antifungal therapy, preferably 14 days following the first negative blood culture. While catheter locks are effective as a preventative measure, their effectiveness as a remedy has not yet been proven. The review comes to the conclusion that *Candida* CRBSI poses a serious risk to HPN patients and emphasises the importance of catheter removal and antifungal therapy as the gold standard of care. However, prophylactic catheter locks and in-situ catheterization treatments seem to be gaining ground as alternatives [25].

Parenteral nutrition before liver transplant in biliary atresia and bloodstream infections

Effects of Parenteral Nutrition (PN) on anthropometric measurements in paediatric liver transplant candidates with End-Stage Liver Disease (ESLD) were examined. Assessing PN problems, liver function tests, waiting duration, and post-transplant length of stay were among the secondary goals. According to the study, PN was successful in treating malnutrition in a sizable percentage of patients, with 39% of patients experiencing improvement in their triceps skinfold thickness and mid-upper arm circumference. The remaining patients' malnutrition either got better or got worse. No patients receiving PN died, however, rates of central line infection were seen. The study found that PN may help children

with ESLD who have failed enteral feeding to improve and/or resolve malnutrition, potentially leading to better liver transplant outcomes [26].

Bariatric surgery and bloodstream infections

Long-term weight loss can be accomplished with great success through bariatric surgery, but there is a risk of surgical issues or severe malabsorption that can result in malnutrition. To treat surgical complications or malnutrition brought on by these procedures, Parenteral Nutrition (PN) may be required. However, there is little information available on the application of Home PN (HPN) in this patient population. In order to find patients who received HPN between January 2003 and August 2015 and had undergone bariatric surgery, a retrospective analysis of an HPN database was carried out. The average age of the 54 HPN patients who were found was 52.1 12.8 years, and 80% of them were female. Malnutrition or failure to thrive was the most frequent cause of HPN (57%), and Roux-en-Y gastric bypass was the most often performed surgical technique (72%). Weight was 71.9 20.4 kg at the beginning of HPN treatment; by the end, it had significantly grown to 78.9 24.4 kg ($p = .0001$). By the end of HPN, serum albumin levels increased from 2.8 0.77 g/dL to 3.7 0.58 g/dL ($p .0001$). 83.3% of patients underwent revision surgery. These retrospective findings conclude that HPN may be a viable nutritional and transitional option for malnourished post-bariatric surgery patients before revision surgery [27].

Urinary tract infections and bloodstream infections

By the age of seven, Urinary Tract Infections (UTIs), which affect more girls (8%) than boys (2%), are a common cause of acute illness in newborns and young children, with a recurrence rate of 10% to 30%. Children with UTIs are susceptible to sepsis and other potentially fatal diseases. The purpose of this study was to estimate the prevalence of UTIs in underweight children. Between July 7, 2019, and January 7, 2020, 241 patients from Swabi, Pakistan's Children Gajju Khan Medical College's Paediatric Department participated in the study. All children had urine samples drawn using catheterization and urine bags, and the samples were forwarded to the hospital's lab for UTI testing. According to the findings, 19 (7.88%) of the patients developed UTIs [28].

Chlorhexidine and povidone-iodine solution-mediated treatment

The effectiveness of chlorhexidine and povidone-iodine solution for vascular catheter-site care. This work contributes significantly to the knowledge base surrounding preventative measures for catheter-induced bloodstream infections. The authors' thorough analysis of existing studies on these two common antiseptic solutions provides an in-depth understanding of their respective efficacy. The findings suggest chlorhexidine's superiority in reducing catheter-related bloodstream infections, offering an evidence-based recommendation for healthcare practice. The strength of this



research lies in its robust methodology and comprehensive approach, summarizing a broad range of studies to deliver conclusive insights. Although the research doesn't specifically focus on Pakistan, its findings are universally relevant, providing valuable information for healthcare professionals and policymakers aiming to reduce catheter-induced bloodstream infections. This meta-analysis is an excellent example of the synthesis of existing knowledge to inform clinical best practices, demonstrating the importance of evidence-based healthcare decision-making [29].

Heparin plus gentamicin catheter lock solution and bloodstream infections

The high occurrence of CRBSIs in hemodialysis patients, which can have serious consequences for morbidity and mortality, is highlighted by the authors in their first paragraph. They mention that one possible tactic to lower the frequency of CRBSIs is the use of antimicrobial lock solutions, such as heparin with gentamicin. The study involved 120 hemodialysis patients with central venous catheters and was a randomised controlled experiment. A catheter lock solution containing heparin and gentamicin was given to one group of patients, while heparin alone was given to the other group of patients. Over a 6-month period, the incidence of CRBSIs was compared between the two groups. According to the study, CRBSIs were considerably less common in the heparin + gentamicin group than in the heparin-only group (6.7% vs. 23.3%). The use of the heparin plus gentamicin lock solution was safe and well-tolerated by the patients, according to the authors. The use of heparin + gentamicin as a catheter lock solution is an efficient tactic, according to the authors, for lowering the incidence of CRBSIs in hemodialysis patients. They advise additional research to be conducted in order to verify these conclusions and determine the ideal frequency and duration of antimicrobial lock treatments. Overall, this paper offers significant insights into a feasible plan for shielding hemodialysis patients against CRBSIs. It's crucial to remember that the study only had a limited sample size and was conducted in a single centre. To verify these results, additional research with bigger sample sizes and multicenter designs is required [30].

The primary recommendations for stakeholders, based on this study, are to prioritize and implement stringent infection control measures within healthcare settings to prevent CRBSIs. This includes ensuring the use of aseptic techniques during catheter insertion, promoting good hand hygiene among healthcare professionals, and maintaining rigorous site care practices. Additionally, it is crucial to judiciously assess the necessity of catheters and promptly remove them when they are no longer required. Special attention should be given to patients with compromised immune systems, as they are more vulnerable to CRBSIs. Moreover, stakeholders should consider investing in educational programs to raise awareness and improve adherence to these infection control

procedures. By following these recommendations, healthcare facilities can significantly reduce the incidence of CRBSIs and enhance patient safety.

Discussion

Rosenthal, et al. 2020, provides a holistic view of catheter-induced bloodstream infections in several Middle East countries, including Pakistan. The six-year-long study is meticulously designed and implemented, covering an extensive sample of 246 intensive units in 83 hospitals across 52 cities. The methodological rigor provides valuable data, illuminating the wide-scale implications of catheter-induced infections. Despite the study covering multiple countries, the data specific to Pakistan is crucial to understanding the national context. The findings expose critical patterns and potential risk factors associated with these infections, offering valuable insights for medical practitioners and policy-makers. Moreover, the authors successfully highlight the urgency to develop effective interventions for infection control, stressing the need for robust health policies. This article underlines the importance of continuous monitoring and data collection to facilitate evidence-based decision-making, thereby improving patient safety and healthcare outcomes. However, as this study groups Pakistan with many other countries, further country-specific research would be beneficial to understand the unique local dynamics better [31].

Haque and his team delve into a topic of paramount importance - device-associated infections in a Paediatric Intensive Care Unit (PICU) in Pakistan. This focused investigation offers critical insights into the high vulnerability of children to such infections, demonstrating the gravity of the situation within paediatric healthcare settings. The authors adopt an in-depth analytical approach, identifying not only the occurrence of these infections but also their associated factors. These findings underscore the pressing need for improved infection control protocols within PICUs. The article is particularly significant due to its specific focus on children, a demographic often sidelined in mainstream research. It also offers a unique contribution to the literature by focusing on the Pakistani context, which typically lacks substantial primary data. However, given its limited geographic coverage (one PICU), further research covering diverse settings would provide a more comprehensive understanding of device-associated infections across Pakistan. Despite this, the study successfully highlights the urgent need for targeted strategies to reduce the incidence and impact of device-associated infections, thus contributing significantly to the discourse on enhancing paediatric healthcare in Pakistan [32-37].

The frequency, clinical presentation, and microbiological spectrum of candidemia at a tertiary care facility in Karachi, Pakistan, are all carefully examined by Kumar and his team in their study. The authors close a significant gap in the body of knowledge by concentrating on candidemia, a region of



catheter-induced bloodstream infections that is frequently understudied. The authors' dedication to analysing the microbiological and clinical components of the illnesses offers a thorough comprehension of the intricacy of the issue. The study's specificity, which offers an in-depth look at the prevalence of candidemia at a single tertiary care facility, could be used as a useful model for similar investigations. The study, however, is limited to a single facility in Karachi, so its conclusions could not apply to other parts of Pakistan. The authors present evidence for the necessity of designing efficient treatments specifically suited to the local microbiological context and improving infection control methods. This study adds significantly to the expanding body of knowledge on catheter-induced bloodstream infections despite its geographical limits by highlighting the significance of a thorough, in-depth analysis of particular types of infections [38].

A significant contribution to the area is made by Farooqi, et al. [39] study of invasive candidiasis in Pakistan, which presents a well-organized analysis of clinical traits, species distribution, and antifungal susceptibility. The study's emphasis on invasive candidiasis, a serious type of bloodstream infection, offers insightful information about this particular health problem in the nation. It is possible to have a thorough grasp of the difficulties associated with treating such infections thanks to the thorough research of several species of *Candida* and their sensitivity to antifungal medications. The authors' findings have been extensively documented, highlighting how challenging it is to treat invasive candidiasis in Pakistani healthcare settings. Given its direct relevance to clinical practise and policy-making, their emphasis on local antifungal susceptibility patterns is particularly praiseworthy. The urgent necessity for ongoing surveillance and customised treatment regimens based on regional susceptibility patterns is also highlighted by this study. Although the study only looked at one type of catheter-induced infection, its findings are nonetheless quite insightful because they do not include all catheter-induced infections. However, it continues to be a crucial tool for medical experts and decision-makers working to develop more efficient plans to fight invasive candidiasis and similar types of other infections in recourse-limited countries like Pakistan [39-46].

By describing the bacterial spectrum and patterns of antibiotic susceptibility, Butt and his team present a focused investigation on bloodstream infections in febrile neutropenic patients. The authors focus on a significant subset of catheter-induced infections among a group of patients who are at risk, offering a carefully organised analysis that clarifies the nuances of these illnesses in the context of Pakistan. The investigation of the bacterial spectrum and the identification of antibiotic susceptibility patterns add significant knowledge to the area and provide crucial insights for the formulation of efficient therapeutic approaches. The research's patient-specific approach, which helps therapies be tailored to the

needs of febrile neutropenic patients, is its main strength. However, because of the particular patient group analysed, the study's results might not be completely generalizable. The findings would be more broadly applicable if there was further research that looked at other patient demographics. Despite this drawback, the work of Butt, et al. [47] offers a critical perspective on bloodstream infections in febrile neutropenic patients in Pakistan and highlights the necessity for tailored, efficient treatment plans based on regional bacterial and antimicrobial patterns [47].

Conclusion

The current study sheds light on the critical issue of catheter-induced bloodstream infections, offering valuable insights and recommendations for healthcare practitioners and policy-makers in Pakistan. There is an urgent need for targeted strategies, evidence-based decision-making, and continuous surveillance to reduce the incidence and impact of catheter-related bloodstream infections in Pakistan. A multifaceted approach, including tailored interventions and rigorous infection control measures, is essential to enhance patient safety and healthcare outcomes in the context of catheter-induced infections in Pakistan. Further research and broader geographical coverage will be beneficial for a more comprehensive understanding of this critical issue.

References

1. Global Burden of Disease 2021 Health Financing Collaborator Network. Global investments in pandemic preparedness and COVID-19: development assistance and domestic spending on health between 1990 and 2026. *Lancet Glob Health*. 2023 Mar;11(3):e385-e413. doi: 10.1016/S2214-109X(23)00007-4. Epub 2023 Jan 24. PMID: 36706770; PMCID: PMC9998276.
2. GBD 2019 Pakistan Collaborators. The state of health in Pakistan and its provinces and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Glob Health*. 2023 Feb;11(2):e229-e243. doi: 10.1016/S2214-109X(22)00497-1. PMID: 36669807; PMCID: PMC10009760.
3. Nejadghaderi SA, Moghaddam SS, Azadnajafabad S, Rezaei N, Rezaei N, Tavangar SM, Jamshidi H, Mokdad AH, Naghavi M, Farzadfar F, Larijani B; GBD 2019 NAME Thyroid Cancer Collaborators. Burden of thyroid cancer in North Africa and Middle East 1990-2019. *Front Oncol*. 2022 Sep 23; 12:955358. doi: 10.3389/fonc.2022.955358. Erratum in: *Front Oncol*. 2023 Apr 28; 13:1208646. PMID: 36212501; PMCID: PMC9538696.
4. Saeed U, Piracha ZZ, Uppal SR, Waheed Y, Uppal R. SARS-CoV-2 induced hepatic injuries and liver complications. *Front Cell Infect Microbiol*. 2022 Sep 16; 12:726263. doi: 10.3389/fcimb.2022.726263. PMID: 36189356; PMCID: PMC9523111.
5. GBD 2019 LRI Collaborators. Age-sex differences in the global burden of lower respiratory infections and risk factors, 1990-2019: results from the Global Burden of Disease Study 2019. *Lancet Infect Dis*. 2022 Nov;22(11):1626-1647. doi: 10.1016/S1473-3099(22)00510-2. Epub 2022 Aug 11. PMID: 35964613; PMCID: PMC9605880.
6. Khalid K, Saeed U, Aljuaid M, Ali MI, Anjum A, Waheed Y. Immunoinformatic Approach to Conceive a Next Generation Multi-Epitope Vaccine Against *Achromobacter xylosoxidans* Infections. *Front Med (Lausanne)*. 2022 Jul 11; 9:902611. doi: 10.3389/fmed.2022.902611.



7. Polaris Observatory HCV Collaborators. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study. *Lancet Gastroenterol Hepatol.* 2022 May;7(5):396-415. doi: 10.1016/S2468-1253(21)00472-6.
8. Fram D, Okuno MF, Taminato M, Ponzio V, Manfredi SR, Grothe C, Belasco A, Sesso R, Barbosa D. Risk factors for bloodstream infection in patients at a Brazilian hemodialysis center: a case-control study. *BMC Infect Dis.* 2015 Mar 26; 15:158. doi: 10.1186/s12879-015-0907-y. PMID: 25879516; PMCID: PMC4377039.
9. Lang R, Gill MJ, Viczko J, Naugler C, Church D. Risk Factors and Outcomes of Bloodstream Infections Among People with Human Immunodeficiency Virus: A Longitudinal Cohort Study from 2000 to 2017. *Open Forum Infect Dis.* 2022 Aug 3; 9(8):ofac318. doi: 10.1093/ofid/ofac318. PMID: 35937645; PMCID: PMC9346145.
10. Ibrahim MK, Zambruni M, Melby CL, Melby PC. Impact of Childhood Malnutrition on Host Defense and Infection. *Clin Microbiol Rev.* 2017 Oct;30(4):919-971. doi: 10.1128/CMR.00119-16. PMID: 28768707; PMCID: PMC5608884.
11. Surapat B, Montakantikul P, Malathum K, Kiertiburanakul S, Santanirand P, Chindavijak B. Microbial epidemiology and risk factors for relapse in gram-negative bacteria catheter-related bloodstream infection with a pilot prospective study in patients with catheter removal receiving short-duration of antibiotic therapy. *BMC Infect Dis.* 2020 Aug 17;20(1):604. doi: 10.1186/s12879-020-05312-z. PMID: 32807092; PMCID: PMC7430115.
12. Paulsen J, Askim Å, Mohus RM, Mehl A, Dewan A, Solligård E, Damås JK, Åsvold BO. Associations of obesity and lifestyle with the risk and mortality of bloodstream infection in a general population: a 15-year follow-up of 64 027 individuals in the HUNT Study. *Int J Epidemiol.* 2017 Oct 1;46(5):1573-1581. doi: 10.1093/ije/dyx091. PMID: 28637260.
13. Hamer M, Kivimäki M, Gale CR, Batty GD. Lifestyle risk factors, inflammatory mechanisms, and COVID-19 hospitalization: A community-based cohort study of 387,109 adults in UK. *Brain Behav Immun.* 2020 Jul; 87:184-187. doi: 10.1016/j.bbi.2020.05.059. Epub 2020 May 23. PMID: 32454138; PMCID: PMC7245300.
14. Buchman AL, Opilla M, Kwasny M, Diamantidis TG, Okamoto R. Risk factors for the development of catheter-related bloodstream infections in patients receiving home parenteral nutrition. *JPEN J Parenter Enteral Nutr.* 2014 Aug;38(6):744-9. doi: 10.1177/0148607113491783. Epub 2013 Jun 6. PMID: 23744839.
15. Davidson JB, Edakkanambeth Varayil J, Okano A, Whitaker JA, Bonnes SL, Kelly DG, Mundi MS, Hurt RT. Prevention of Subsequent Catheter-Related Bloodstream Infection Using Catheter Locks in High-Risk Patients Receiving Home Parenteral Nutrition. *JPEN J Parenter Enteral Nutr.* 2017 May;41(4):685-690. doi: 10.1177/0148607115604118. Epub 2015 Sep 2. PMID: 26334797.
16. Calder PC, Carr AC, Gombart AF, Eggersdorfer M. Optimal Nutritional Status for a Well-Functioning Immune System Is an Important Factor to Protect against Viral Infections. *Nutrients.* 2020 Apr 23;12(4):1181. doi: 10.3390/nu12041181. PMID: 32340216; PMCID: PMC7230749.
17. Szeinbach SL, Pauline J, Villa KF, Commerford SR, Collins A, Seoane-Vazquez E. Evaluating catheter complications and outcomes in patients receiving home parenteral nutrition. *J Eval Clin Pract.* 2015 Feb;21(1):153-9. doi: 10.1111/jep.12264. Epub 2014 Nov 6. PMID: 25377903.
18. Xue Z, Coughlin R, Amorosa V, Quinn R, Schiavone P, Stoner N, Kinoshian B, Compher C. Factors Associated with Central Line-Associated Bloodstream Infections in a Cohort of Adult Home Parenteral Nutrition Patients. *JPEN J Parenter Enteral Nutr.* 2020 Nov;44(8):1388-1396. doi: 10.1002/jpen.1876. Epub 2020 Jun 10. PMID: 32386254.
19. Vashi PG, Virginkar N, Popiel B, Edwin P, Gupta D. Incidence of and factors associated with catheter-related bloodstream infection in patients with advanced solid tumors on home parenteral nutrition managed using a standardized catheter care protocol. *BMC infectious diseases.* 2017; 17(1):1-9.
20. Demirci R, Sahtiyanci B, Bakan A, Akyuz O. The predictors of catheter-related bloodstream infections in patients undergoing hemodialysis: A single center experience. *J Vasc Access.* 2023 Jan;24(1):76-81. doi: 10.1177/1129729821998836. Epub 2021 Jun 17. PMID: 34137310.
21. Yaqub S, Abdul Razzaque MR, Aftab A, Siddiqui NA. Outcomes of tunneled cuffed hemodialysis catheters: An experience from a tertiary care center in Karachi, Pakistan. *J Vasc Access.* 2022 Mar;23(2):275-279. doi: 10.1177/1129729821989904. Epub 2021 Jan 23. PMID: 33487073.
22. Rashid S, Quershi M, Moon F, Qamar M, Danial K. Frequency of Catheter Infections in Patients of Hemodialysis Despite Using Antibiotic Lock: Catheter Infections Despite Using Antibiotic Lock. *Pakistan Journal of Health Sciences.* 2022; 219-223.
23. Tamura A, Minami K, Tsuda Y, Mizumoto K, Suzuki H. Adolescent eating disorder with catheter-related bloodstream infection. *Pediatr Int.* 2021 Jun;63(6):678-684. doi: 10.1111/ped.14511. Epub 2021 Apr 28. PMID: 33053266.
24. Ulu-Kilic A, Gundogdu A, Cevahir F, Kilic H, Gunes T, Alp E. An outbreak of bloodstream infection due to extensively resistant *Acinetobacter baumannii* among neonates. *Am J Infect Control.* 2018 Feb;46(2):154-158. doi: 10.1016/j.ajic.2017.08.007. Epub 2017 Sep 25. PMID: 28958447.
25. Phua AI, Hon KY, Holt A, O'Callaghan M, Bihari S. Candida catheter-related bloodstream infection in patients on home parenteral nutrition - Rates, risk factors, outcomes, and management. *Clin Nutr ESPEN.* 2019 Jun;31:1-9. doi: 10.1016/j.clnesp.2019.03.007. Epub 2019 Apr 5. PMID: 31060825.
26. Wendel D, Mortensen M, Harmeson A, Shaffer ML, Hsu E, Horslen S. Resolving Malnutrition With Parenteral Nutrition Before Liver Transplant in Biliary Atresia. *J Pediatr Gastroenterol Nutr.* 2018 Feb;66(2):212-217. doi: 10.1097/MPG.0000000000001798. PMID: 29356765.
27. Mundi MS, Vallumsetta N, Davidson JB, McMahon MT, Bonnes SL, Hurt RT. Use of Home Parenteral Nutrition in Post-Bariatric Surgery-Related Malnutrition. *JPEN J Parenter Enteral Nutr.* 2017 Sep;41(7):1119-1124. doi: 10.1177/0148607116649222. Epub 2016 May 13. PMID: 27208038.
28. Sijad-Ur-Rehman BN, Ishaq M, Ullah K, Lala G, Bibi R. Infection of the Urinary Tract and its Prevalence Among Children Presenting with Malnutrition. *Pakistan Journal of Medical & Health Sciences.* 2022.; 16(04):857-857.
29. Chaiyakunapruk N, Veenstra DL, Lipsky BA, Saint S. Chlorhexidine compared with povidone-iodine solution for vascular catheter-site care: a meta-analysis. *Ann Intern Med.* 2002 Jun 4;136(11):792-801. doi: 10.7326/0003-4819-136-11-200206040-00007. PMID: 12044127.
30. Dogra GK, Herson H, Hutchison B, Irish AB, Heath CH, Golledge C, Luxton G, Moody H. Prevention of tunneled hemodialysis catheter-related infections using catheter-restricted filling with gentamicin and citrate: a randomized controlled study. *J Am Soc Nephrol.* 2002 Aug;13(8):2133-9. doi: 10.1097/01.asn.0000022890.29656.22. PMID: 12138146.
31. Rosenthal VD, Belkebir S, Zand F, Afeef M, Tanzi VL, Al-Abdely HM, El-Kholy A, Aziz AIKhwaja SA, Demiroz AP, Sayed AF, Elahi N, Gamar-Elanbya MO, Abidi K, Ben-Jaballah N, Salama MF, Helali NJ, Abdel-Halim MM, Demaisip NL, Ahmed H, Diab HH, Molano AM, Sawan FA, Kelany A, Altowerqi R, Rushdi H, Alkamaly MA, Bohlega E, Aldossary HA, Abdelhady KM, Ikram A, Madco M, Caminade Y, Alazmi M, Mahfouz T, Abdelaziz-Yousef RH, Ibrahim A, Elawady B, Asad T, Shyrine L, Leblebicioglu H. Six-year multicenter study on short-term peripheral venous catheters-related bloodstream infection rates in 246 intensive units of 83 hospitals in 52 cities of 14 countries of Middle East: Bahrain, Egypt, Iran, Jordan, Kingdom of Saudi Arabia, Kuwait, Lebanon, Morocco, Pakistan, Palestine, Sudan, Tunisia, Turkey, and United Arab Emirates-International Nosocomial Infection



- Control Consortium (INICC) findings. *J Infect Public Health*. 2020 Aug;13(8):1134-1141. doi: 10.1016/j.jiph.2020.03.012. Epub 2020 Apr 12. PMID: 32295756.
32. Haque A, Ahmed SA, Rafique Z, Abbas Q, Jurair H, Ali SA. Device-associated infections in a paediatric intensive care unit in Pakistan. *J Hosp Infect*. 2017 Jan;95(1):98-100. doi: 10.1016/j.jhin.2016.10.021. Epub 2016 Nov 4. PMID: 27890335.
 33. Qamar MU, Rizwan M, Uppal R, Khan AA, Saeed U, Ahmad K, Iqbal MJ, Ali Z, Suleman M. Antimicrobial susceptibility and clinical characteristics of multidrug-resistant polymicrobial infections in Pakistan, a retrospective study 2019-2021. *Future Microbiol*. 2023 Oct 26. doi: 10.2217/fmb-2023-0110. Epub ahead of print. PMID: 37882773.
 34. Polaris Observatory Collaborators. Global prevalence, cascade of care, and prophylaxis coverage of hepatitis B in 2022: a modelling study. *Lancet Gastroenterol Hepatol*. 2023 Oct;8(10):879-907. doi: 10.1016/S2468-1253(23)00197-8. Epub 2023 Jul 27. PMID: 37517414.
 35. Piracha ZZ, Saeed U, Ahmed RA, Khan FN, Nasir MI. Global emergence of Langya virus: A serious public health concern. *J Glob Health*. 2023 Jul 7; 13:03034. doi: 10.7189/jogh-13-03034. PMID: 37411008; PMCID: PMC10325733.
 36. National Institute for Health and Care Research Global Health Research Unit on Global Surgery. Reducing the environmental impact of surgery on a global scale: systematic review and co-prioritization with healthcare workers in 132 countries. *Br J Surg*. 2023 Jun 12;110(7):804-817. doi: 10.1093/bjs/znad092. Erratum in: *Br J Surg*. 2023 Sep 22; PMID: 37079880; PMCID: PMC10364528.
 37. Saeed U, Piracha ZZ. PIN1 and PIN4 inhibition via parvulin impeded Juglone, PiB, ATRA, 6,7,4'-THIF, KPT6566, and EGCG thwarted hepatitis B virus replication. *Front Microbiol*. 2023 Jan 25; 14:921653. doi: 10.3389/fmicb.2023.921653.
 38. Kumar S, Kalam K, Ali S, Siddiqi S, Baqi S. Frequency, clinical presentation and microbiological spectrum of candidemia in a tertiary care center in Karachi, Pakistan. *J Pak Med Assoc*. 2014 Mar;64(3):281-5. PMID: 24864600.
 39. Farooqi JQ, Jabeen K, Saeed N, Iqbal N, Malik B, Lockhart SR, Zafar A, Brandt ME, Hasan R. Invasive candidiasis in Pakistan: clinical characteristics, species distribution and antifungal susceptibility. *J Med Microbiol*. 2013 Feb;62(Pt 2):259-268. doi: 10.1099/jmm.0.048785-0. Epub 2012 Oct 25. PMID: 23105021; PMCID: PMC4629241.
 40. Saeed U, Piracha ZZ, Kwon H, Kim J, Kalsoom F, Chwae YJ, Park S, Shin HJ, Lee HW, Lim JH, Kim K. The HBV Core Protein and Core Particle Both Bind to the PPIase Par14 and Par17 to Enhance Their Stabilities and HBV Replication. *Front Microbiol*. 2021 Dec 14; 12:795047. doi: 10.3389/fmicb.2021.795047. PMID: 34970249; PMCID: PMC8713550.
 41. Saeed U, Uppal SR, Piracha ZZ, Uppal R. SARS-CoV-2 Spike Antibody Levels Trend among Sinopharm Vaccinated People. *Iran J Public Health*. 2021 Jul;50(7):1486-1487. doi: 10.18502/ijph.v50i7.6640. PMID: 34568189; PMCID: PMC8426791.
 42. Saeed U, Kim J, Piracha ZZ, Kwon H, Jung J, Chwae YJ, Park S, Shin HJ, Kim K. Parvulin 14 and Parvulin 17 Bind to HBx and cccDNA and Upregulate Hepatitis B Virus Replication from cccDNA to Virion in an HBx-Dependent Manner. *J Virol*. 2019 Mar 5; 93(6):e01840-18. doi: 10.1128/JVI.01840-18. PMID: 30567987; PMCID: PMC6401437.
 43. Piracha ZZ, Kwon H, Saeed U, Kim J, Jung J, Chwae YJ, Park S, Shin HJ, Kim K. Sirtuin 2 Isoform 1 Enhances Hepatitis B Virus RNA Transcription and DNA Synthesis through the AKT/GSK-3 β -Catenin Signaling Pathway. *J Virol*. 2018 Oct 12; 92(21):e00955-18. doi: 10.1128/JVI.00955-18.
 44. Saeed U, Waheed Y, Ashraf M, Waheed U, Anjum S, Afzal MS. Estimation of Hepatitis B Virus, Hepatitis C Virus, and Different Clinical Parameters in the Thalassaemic Population of Capital Twin Cities of Pakistan. *Virology (Auckl)*. 2015 Nov 5; 6:11-6. doi: 10.4137/VRT.S31744. PMID: 26568681; PMCID: PMC4636113.
 45. Waheed Y, Saeed U, Anjum S, Afzal MS, Ashraf M. Development of Global Consensus Sequence and Analysis of Highly Conserved Domains of the HCV NS5B Prote in. *Hepat Mon*. 2012 Sep;12(9):e6142. doi: 10.5812/hepatmon.6142. Epub 2012 Sep 25. PMID: 23087757; PMCID: PMC3475062.
 46. Safi SZ, Waheed Y, Sadat J, Solat-UI-Islam, Salahuddin S, Saeed U, Ashraf M. Molecular study of HCV detection, genotypes and their routes of transmission in North West Frontier Province, Pakistan. *Asian Pac J Trop Biomed*. 2012 Jul;2(7):532-6. doi: 10.1016/S2221-1691(12)60091-4. PMID: 23569965; PMCID: PMC3609335.
 47. Butt T, Afzal RK, Ahmad RN, Salman M, Mahmood A, Anwar M. Bloodstream infections in febrile neutropenic patients: bacterial spectrum and antimicrobial susceptibility pattern. *J Ayub Med Coll Abbottabad*. 2004 Jan-Mar;16(1):18-22. PMID: 15125174.