Review of Contemporary Philosophy
ISSN: 1841-5261, e-ISSN: 2471-089X
Vol 22 (1), 2023
Pp 5558 - 5569

Biosafety and Risk Management Protocols in Clinical Laboratories: Review of Historical Challenges and Future Directions in the Context of Emerging Infectious Diseases

[1]Fahad Hadram Al Harbi ,[2]Rayan Defulla Al Amri ,[3]Khaled Ghali Al Alwi ,[4]Hatem Rashed Al Ruheli ,[5]Mohammad Ghali AlAlwi ,[6]Majed Sayed Al Offi , [7]Faris Mohammad Naser Nahas

1. (Madinah Central Blood Bank)
2. (Madinah Central Blood Bank)
3. (Madinah Central Blood Bank)
4. (Madinah Central Blood Bank)
5. (Madinah Central Blood Bank)
6. (Ohd Hospital in Madinah)
7. (Medical Report in Madinah)

Abstract

Background: Clinical laboratories are essential for patient care and public health, particularly during infectious disease outbreaks. The 2014 Ebola outbreak highlighted significant deficiencies in biosafety protocols within clinical laboratories, which adversely affected patient outcomes. This study explores the challenges and current state of biosafety and risk management in clinical laboratories, particularly in light of recent pandemics.

Methods: A comprehensive review of literature and guidelines related to laboratory biosafety was conducted, focusing on incidents during the Ebola and COVID-19 outbreaks. The analysis included regulatory frameworks, existing biosafety protocols, and case studies demonstrating lapses in safety measures.

Results: Findings indicate that many clinical laboratories operate under minimal regulatory oversight, particularly those with a CLIA Certificate of Waiver. A lack of standardized biosafety practices has been identified, leading to increased risks of laboratory-acquired infections (LAIs). The review also revealed that public health laboratories, while better equipped, still face challenges in maintaining biosafety standards due to resource constraints and the rapid emergence of new infectious agents.

Conclusion: The study underscores the urgent need for enhanced biosafety protocols and regulatory frameworks in clinical laboratories to mitigate risks associated with emerging infectious diseases. Collaborative efforts among healthcare professionals, regulatory bodies, and laboratory experts are essential to develop comprehensive strategies that ensure the safety of laboratory personnel and the reliability of diagnostic testing.

Keywords: Clinical laboratories, biosafety, infectious diseases, regulatory frameworks, laboratory-acquired infections.

Received: 13 october 2023 **Revised:** 27 November 2023 **Accepted:** 11 December 2023

1. Introduction

Patient care and public health rely on the dependability and quality of clinical laboratory testing, since laboratory tests are the most often prescribed diagnostic procedures in all patient interactions. Annually, it is estimated that one-third of the 500 million patient contacts within primary care or outpatient settings require the requisition of one or more laboratory tests (1). Research indicates that a minimum of 50 to 70%

of contemporary medical choices are affected by laboratory test outcomes (2, 3). Preserving clinical laboratory services during an epidemic of a new infectious disease is crucial for patient treatment.

The 2014 Ebola outbreak underscored the necessity for established policies and procedures to protect healthcare workers and emphasized that the consideration of Ebola should not impede diagnostic evaluations, laboratory testing, or the implementation of suitable care for other, more probable medical conditions (4). The 2016 Zika virus epidemic exemplified an emerging infectious illness that developed into a public health disaster, prompting scientists to propose the potential emergence of other viruses in the near future (5–7). During the Zika outbreak, the Clinical Laboratory Improvement Advisory Committee (CLIAC) of the Department of Health and Human Services identified clinical laboratory biosafety as a "critical unmet national need" and urged government to significantly enhance guidance, training, and outreach regarding biosafety for the clinical laboratory community. Consequently, enhancing biosafety management and readiness in clinical labs, which play a crucial role in diagnosing disease outbreaks, is essential for safeguarding public health. The COVID-19 epidemic has once again highlighted the challenges faced by healthcare staff, laboratory personnel, and the public. This research does not concentrate on an extensive examination of biosafety concerns during the current pandemic, since we are still experiencing the epidemic at the time of publishing, making a retrospective analysis unfeasible. The deficiencies shown during the Ebola epidemic remain pertinent in the context of the current pandemic.

In late 2014, at the peak of the Ebola outbreak, concerns over safety in clinical labs directly affected patient care (8). Regrettably, numerous non-Ebola patients exhibiting symptoms, travel histories, or racial and ethnic backgrounds indicative of potential Ebola infection experienced adverse consequences due to apprehensions regarding the management of specimens containing the Ebola virus in diagnostic laboratories lacking appropriate containment measures. Research by the Centers for Disease Control and Prevention (CDC) indicated that at least two individuals, who tested negative for Ebola but had significantly delayed diagnosis and treatment, succumbed to other curable conditions. This investigation identified many instances, as reported by health departments or healthcare practitioners, where the establishment of alternate diagnoses was impeded or postponed owing to concerns over Ebola-related infection management (9,10). A subsequent study recorded instances where apprehensions from health care providers and laboratories regarding potential Ebola exposure hindered the proper application of existing malaria diagnostic and treatment protocols, leading to improper patient evaluation and management practices (11).

Moreover, apprehension over Ebola resulted in several commercial diagnostic labs declaring their unwillingness to handle specimens from patients exhibiting symptoms like to those of Ebola (11, 12). Simultaneously, several laboratory equipment makers advised the incineration of their instruments post-use with Ebola specimens and prohibited their staff from servicing devices used with such specimens (12).

The Ebola epidemic response revealed significant inconsistencies among the recommendations for managing patients with emerging infectious diseases and their specimens, leading to misunderstanding among healthcare workers, including laboratory specialists, over preparation and response protocols. For several individuals, Ebola signified a "absolute risk" that surpassed the need to provide patient care (13). Ambiguity about self-protection and safeguarding colleagues created ethical issues for several healthcare and clinical laboratory workers (13). This Ebola epidemic was confined to a restricted number of suspected patients (4), and state and national public health labs effectively managed the testing requirements.

The CDC/National Institutes of Health's (NIH) Biosafety in Microbiological and Biomedical Laboratories (BMBL), now in its 6th edition, is a well-recognized laboratory biosafety guideline (14). The BMBL emphasizes biological research environments in which the agent is often identified prior to the commencement of the study. This viewpoint significantly contrasts with that of clinical laboratory personnel, who often lack knowledge about the presence of developing diseases or infectious organisms in their specimens. Furthermore, unlike diagnostic labs (15), research laboratories often handle substances at elevated concentrations and substantial quantities.

In acknowledgment of these distinctions, a Biosafety Blue Ribbon Panel organized by the CDC released the "Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories" in 2012 (15). The description of prevalent dangers and the provision of guidelines for safe work practices in diagnostic labs emphasized the correlation between biological agents and biosafety levels. Both the BMBL and this publication stipulate that research involving Ebola must be conducted in a biosafety level four (BSL-4) or maximum containment facility. Given that the majority of clinical laboratories function at biosafety level two (BSL-2), apprehensions regarding biosafety risks and potential exposure partially contributed to the documented hesitance and delays in conducting laboratory tests on suspected Ebola specimens during the 2014 outbreak. Testing a single specimen from a suspected patient, especially one with an uncertain—and potentially minimal—probability of having Ebola virus disease (EVD), entails significantly different risks compared to handling Ebola in a research environment, which may involve large quantities and high concentrations (13). Numerous clinical labs in 2014 internationally, shown their capability to effectively manage such hazards without dependence on a maximum containment laboratory (16, 17). Refer to the section under "Real-life example of biosafety risk management—experience of a community hospital laboratory during an outbreak situation" for an illustration of how a hospital achieved this.

The complexities of clinical laboratory biosafety are further exacerbated by the many types of labs doing medical tests. These encompass national, state, and local public health laboratories, whose results are utilized for direct patient care, disease surveillance, and other public health and epidemiological purposes; large national reference laboratories; and both large and small hospital laboratories catering to specific acute-care populations, as well as physicians' offices and waived-testing sites. Each of them caters to distinct patient demographics, executes diverse treatments with varying risks, and has differing personnel levels and resources. The mobility of populations and the interconnectedness of global food and supply systems facilitate the potential for disease emergence in many locations. Consequently, smaller labs may find themselves in a particularly challenging predicament. They may lack access to specialized knowledge and have personnel with numerous responsibilities (such as microbiological testing and quality management or transfusion testing and laboratory safety), which might demand concessions in risk assessment and biosafety enhancement practices.

"Clinical laboratories" denote facilities mainly dedicated to facilitating direct patient treatment, while "public health laboratories" refer to governmental laboratories at the national, state, and municipal levels, primarily responsible for disease monitoring. We differentiate between diagnostic labs, including both clinical and public health laboratories that conduct testing for direct patient treatment, and research laboratories, which largely generate new information not used for immediate patient decision-making. Public health labs often do both research and diagnostic testing; in reality, these differences often become indistinct.

This analysis illustrates the intricacies and distinctive features of clinical labs, highlighting the difficulty associated with implementing existing biosafety guidelines, particularly in the context of new infectious disease responses. These problems highlight the disparity indicating that prior research has mostly concentrated on academic and industrial methodologies, neglecting the practical realities and safety hazards inherent in clinical laboratory operations. This study does not aim to address all the difficulties related to clinical laboratory biosafety; it is not an advice paper. It underscores the intricacy of the issues and the necessity to pinpoint strategies and resources to concentrate the collective endeavors of the clinical laboratory community, the laboratory safety community, and all stakeholders, to formulate dependable, consistent guidance and secure the support required to enhance clinical laboratory biosafety.

The safety of clinical laboratories directly influences patient safety and public health, warranting significant consideration. This evaluation aims to identify biosafety deficiencies and issues in clinical labs, as well as to outline requirements and potential for improvement. Clinical labs are distinct settings that use tools, techniques, and workflows not often seen in research or academic laboratories. Clinical laboratory biosafety differs from research laboratory biosafety, clinical infection prevention and control, and general safety protocols. The dangers vary, even when the biological agents are sometimes same. Furthermore, clinical labs must consistently acknowledge their direct and immediate responsibility in patient care—a

consideration that research laboratories often do not need to address. Clinical labs must meticulously assess their many requirements, including worker safety and patient care, while acknowledging the inseparable connection between laboratory safety and quality. The attainment of precise and dependable diagnostic test outcomes fundamentally relies on establishing a system capable of efficiently managing hazards to laboratory personnel, healthcare facilities, the general populace, animals, and the environment (4).

2. Biological Risks in Clinical Laboratories

Prior to the establishment of the microbiological genesis of human diseases, researchers studying infectious diseases often contracted these illnesses, either by accidental or intentional exposure during their investigations (18, 19). The identification of a novel etiological agent was often promptly followed by the report of a laboratory-acquired case (19). Significant research on microbiological safety, including the possible hazards of several laboratory operations, originates from the 1950s (20). The advancement of laboratory testing to enhance clinical treatment, alongside the evolution of clinical labs, led to the acknowledgment that personnel in these laboratories faced the chance of exposure to infectious microorganisms. A 1979 study of laboratory-acquired illnesses (LAIs), using data from publications and postal questionnaires, detailed infections caused by bacteria, viruses, fungi, and parasites. While the absence of data for uninfected individuals complicates the evaluation of overall risk, the review indicated that approximately 34% (from 1,342 cases analyzed in 1951) and 17% (from 3,921 cases analyzed in 1976) of total laboratory-acquired infections (LAIs) were linked to clinical rather than research laboratories (21). These LAIs were attributed to a diverse array of infections, with hepatitis being especially common among clinical laboratory personnel.

Exposure to infectious pathogens is a significant public health challenge globally. A 2017 worldwide analysis on incidence, prevalence, and years lived with disability revealed that about 43.2 million years of impairment were attributable to infectious illnesses (22). In the year 2000, it was estimated that there were 926,000 hepatitis C virus (HCV), 2,100,000 hepatitis B virus (HBV), and 327,000,000 human immunodeficiency virus (HIV) exposures among healthcare workers due to percutaneous injuries, leading to 16,000 HCV, 66,000 HBV, and 1,000 HIV infections. Bacterial and fungal infections, such as those caused by *Brucella* spp., *Neisseria meningitidis*, and *Coccidioides* spp., provide a considerable risk for acquired infection (23,24). Among the three primary blood-borne pathogens (HIV, HBV, and HCV), postexposure prophylaxis, hepatitis immunization, and low transmission rates have effectively reduced exposure hazards; nonetheless, deficiencies persist, especially concerning HCV (25, 26).

In the nonmicrobiology segments of clinical labs, a significant concern may be the insufficient understanding of potential infectious agents present in a specimen, leading to inadequate attention to infection risk. This misconception may pose significant challenges in laboratories that create novel testing methodologies, such as molecular and biochemical assays, without thoroughly evaluating the biorisks linked to the specimens, or in point-of-care (POC) testing environments where personnel conducting these tests may lack sufficient training in laboratory protocols and biosafety measures (27).

3. Guidelines and Requirements for Laboratory Biosafety

In 1974, the CDC released "Classification of Etiologic Agents on the Basis of Hazard," which established ideas such containment levels and agent risk groups; with adjustments, this categorization of pathogens aligns with those used today (28). In 1974, the NIH released "National Cancer Institute Safety Standards for Research Involving Oncogenic Viruses," which delineated three containment levels predicated on a risk assessment for virally produced cancer in humans (29). In 1976, the NIH released "Guidelines for Research Involving Recombinant DNA Molecules," outlining the microbiological techniques, equipment, and facility precautions associated with the four levels of physical containment (30). In 1978, a laboratory-associated epidemic of smallpox in the United Kingdom led to the death of Janet Parker, the last human fatality from the illness. Her death prompted a governmental investigation that scrutinized safety protocols in labs engaged in research on hazardous pathogens (31). This episode undoubtedly stimulated the formulation of extensive guidelines for laboratory biosafety. In 1983, the World Health Organization (WHO) released

laboratory safety recommendations, followed by the CDC/NIH in 1984. These rules lacked governmental enforcement but offered a progressive framework for biosafety practices. These fundamental biosafety advice publications mostly focused on biological research environments, where safety issues were deemed most critical.

Beginning in the 1980s, the HIV epidemic heightened awareness of occupationally acquired illnesses, particularly among clinical laboratory personnel. From 1985 to 2013, there were 16 confirmed and 21 probable HIV infections among laboratory professionals, while nurses had 24 confirmed and 37 possible cases (32,33). In 1989, there were 1,304,880 registered nurses and licensed practical nurses, however there were only 140,730 medical technologists and medical laboratory technicians (34–36). A study of proven and potential cases revealed that laboratory professionals acquired 26.3 HIV infections per 100,000, but nurses had just 4.7 infections per 100,000. Consequently, the probability of unintentional infection for laboratory workers was about fivefold greater than that of nurses. A possible reason for this disparity is that clinical laboratory staff may process hundreds of patient specimens daily, which may harbor one or more infectious organisms.

In 1985, the CDC developed "Universal Precautions" to mitigate the spread of blood-borne diseases resulting from exposure to blood and other potentially infectious materials (37–42). In 1991, the workplace Safety and Health Administration (OSHA) established a regulation requirement to mitigate or eradicate workplace exposure to blood-borne infections (43). In 1996, the CDC's "Guideline for Isolation Precautions in Hospitals" integrated Universal Precautions with earlier recommendations on body substance isolation, now termed "Standard Precautions." This guideline also introduced three categories of "Transmission-Based Precautions": airborne, droplet, and contact. The revised recommendations apply to the management of all patients, regardless of their medical condition or the possible mode of exposure to healthcare workers (42). The OSHA blood-borne pathogen standard was amended in 2000 to mandate that employers use procedures to eradicate or reduce exposure to contaminated sharps (44). Consequently, due to these governmental initiatives, verified occupationally acquired HIV infections plummeted from a high of eight cases in 1992 to only one case recorded between 2000 and 2013 (33).

The September 11, 2001, events and the ensuing anthrax attacks in the United States heightened scrutiny on laboratory biosafety, particularly in the emerging domain of "laboratory biosecurity." In 2002, the federal Select Agent Rule was amended to mandate that any facility housing select agents register with the government and adopt measures to safeguard those agents. The amended Select Agent Rule referenced the BMBL and established an expectation for select agent labs to adhere to that advice (45). In 2012, the Select Agent Rule was amended to implement security measures for select agents and to decrease the total number of agents on the comprehensive list. The Select Agent Rule was revised in 2016 to include Bacillus cereus biovar anthracis. In 2018, 253 organizations were registered with the Federal Select Agent Program (46).

Notwithstanding the significant decline in occupationally acquired HIV infections throughout the 1990s and 2000s, apprehensions persisted over the frequency of laboratory exposures, which were believed to be more prevalent than commonly assumed (33, 47). Data on exposures and LAIs remains elusive or fragmentary due to the reliance on retrospective assessments, pathogen-specific investigations, volunteer reporting, anecdotal evidence, and the absence of an official monitoring system (33, 48). This renders it unfeasible to precisely assess the optimal strategies for preventing accidents, exposures, and infections in a clinical laboratory environment. Despite the 2012 “Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories” recommending the establishment of a “central site for surveillance and nonpunitive reporting of laboratory incidents/exposures, injuries, and infections” (15), such a surveillance system remains nonexistent today. Additionally, 2018 research conducted by The National Academy of Sciences highlighted the need for enhanced occupational safety and health monitoring across all workplaces (49). Recently, the American Biological Safety Association International (ABSA) established a searchable database that monitors LAIs documented in the literature (50). Nonetheless, the quantity, contexts, and attributes of unreported episodes throughout the country mostly remain undisclosed.

Since 2012, laboratory biosafety has persisted in the national discourse, particularly regarding the legitimacy of gain-of-function research on avian influenza, the transmission of inadequately inactivated anthrax from the Army's Dugway Proving Ground, the identification of smallpox virus at the NIH campus, and two distinct laboratory incidents involving *Bacillus anthracis* (the causative agent of anthrax) and Ebola virus that occurred at the CDC in 2014 (51–53). Federal reactions to these incidents have been concentrated on high-containment research institutions (i.e., biosafety level three [BSL-3] or BSL-4) that handle select agents. In 2014, the White House declared the government's obligation to guarantee the safe and secure conduct of infectious disease research, and began a "safety stand-down" along with a "immediate sweep" of federal sites to detect select agents (54). The Federal Experts Security Advisory Panel (FESAP) was rechartered to assess strategies for improving biosafety and biosecurity in high-containment facilities that handle select agents; a plan to execute the FESAP's recommendations was released in 2015 (55). However, such suggestions mostly omitted the evaluation of diagnostic labs. This viewpoint is also apparent in a comprehensive series of publications about the safety and regulation of high-containment labs (56).

Public health laboratories in the nation hold a distinctive role, as the majority conduct clinical and/or diagnostic testing and are governed by the Clinical Laboratory Improvement Amendments (CLIA) (57). Furthermore, many of these laboratories constitute the foundation of the Laboratory Response Network (LRN), established to address emerging disease strains, natural disasters, chemical incidents, foodborne outbreaks, and various health emergencies. The LRN network normally comprises 120 to 130 reference labs, the majority of which has supplementary containment capabilities, typically BSL-3, and are registered with the Federal Select Agent Program (58). In response to the biosafety concerns raised during the 2014 Ebola outbreak, the CDC allocated funding from 2016 to 2018, including the Public Health Emergency Preparedness (PHEP) cooperative agreement, to improve laboratory biosafety and biosecurity in state, local, and territorial public health laboratories (59). This financing facilitated the hiring of biosafety experts and increased the availability of biosafety resources and training within public health labs during a two-year period. In addition to this provisional government aid, the public health and clinical labs have obtained little targeted help to enhance laboratory biosafety (60).

4. Contemporary Regulatory Supervision for Biosafety in Clinical Laboratories

Over 260,000 clinical labs are accredited under CLIA requirements; however, over 75% of these laboratories are subject to little regulatory scrutiny since they operate under a CLIA Certificate of Waiver and do not get regular inspections. The CLIA regulatory criteria applicable to the other 25% of labs emphasize the quality and reliability of clinical laboratory tests, including only basic safety requirements for laboratories (57). CLIA inspections primarily concentrate on laboratory quality rather than biosafety, since regulatory compliance is evaluated by CLIA surveyors or inspectors. While CLIA mandates that a laboratory's environment be suitable for the tests conducted and that people be safeguarded against risks, it does not explicitly address biosafety or delineate the design or implementation of laboratory safety systems. CLIA regulations assign the laboratory director the responsibility of ensuring a safe environment that protects employees from physical, chemical, and biological hazards, as well as establishing appropriate policies and procedures, including the mandates for conducting competency assessments of personnel (61-63). The interpretation of these basic safety rules relies on the competence of laboratory specialists and the inspectors conducting the evaluations. Consequently, clinical laboratory safety may not be uniformly implemented throughout the country (64,65).

5. Common Issues in The Clinical Laboratory

Clinical labs are at the forefront of infectious illnesses and epidemics. They are tasked with identifying the etiological agent responsible for the illness and being vigilant to detect an epidemic (66). Biosafety considerations in clinical labs differ from those in research or public health institutions, since each material poses an unidentified risk, and the presumed diagnosis is often not disclosed to the laboratory. Consequently, substantial dangers to public health arise when clinical labs are unable to properly analyze specimens from patients with, or suspected of having, highly contagious disorders.

6. Research on laboratory contamination

Research into the contamination of laboratory equipment has shown many possible risks. Research used mouse liver homogenates together recombinant herpes simplex virus to assess laboratory contamination using an ultrasonic processor and a tissue dispenser (67). This investigation revealed that these gadgets, under typical use, produced aerosols containing live virus. A further investigation examined clinical laboratory contamination with human rhinovirus under standard operational procedures (68). Samples were taken from personal protective equipment and laboratory apparatus used for viral collection and processing. Viral contamination was identified on the glove and cuff of protective attire, as well as inside the BSC windows, garbage handles, the inner walls of the centrifuge, and the internal surface of the centrifuge rotor.

A distinct investigation examined HBV and HCV contamination by obtaining swab samples from a fully automated laboratory system in a clinical setting. The swab samples were examined, revealing the greatest levels of pathogen contamination at tube manipulation points and the decapper waste chute. Research using fluorescent dye and bacteriophage to evaluate contamination among laboratory personnel, testing apparatus, and a biosafety cabinet revealed a significant level of contamination, with 16% of technologists ungloved hands affected, despite the usage of gloves (69). They specifically evaluated a commercial device that provides rapid cartridge-based assays for the detection of nucleic acids, including Ebola RNA; a rapid malaria antigen assay; and a point-of-care instrument commonly utilized in containment laboratories for handling Ebola virus-infected specimens. They significantly reduced, but did not eradicate, contamination by altering their process and using double gloving (69).

7. Personal Protective Equipment for Clinical Laboratories

Personal Protective Equipment (PPE) refers to particular attire or gear used by clinical laboratory staff to safeguard against contagious and dangerous substances (70). Although critical to the biosafety community and extensively used, the availability of personal protective equipment (PPE) in clinical labs is often inadequate, as are the mechanisms for assuring its proper usage. Consequently, several clinical labs have adhered to recommendations from the CDC and other organizations in formulating a strategy for managing PPE, which included training on equipment use and competence evaluation.

The CDC delineated the principles of PPE use during direct patient interaction with suspected infectious fluids in the Ebola healthcare advice (71), which are similarly applicable to other dangers. This guideline offers suggestions for the application of PPE, its use during patient care, and its removal. The CDC advises that a certified observer should oversee the proper sequence of wearing to prevent any alterations after entering the patient care area. It is essential to maintain the use of PPE throughout the whole length of patient care. Upon a breach in personal protective equipment, the healthcare professional should promptly go to the doffing area to evaluate exposure.

The methods of double gloving and removing contaminated outer gloves, as opposed to sanitizing gloved hands, have both been proposed; nevertheless, there is discrepancy in the advise of the efficacy of each (42, 72,73). Owing to the absence of agreement in the research and the variability in institutional risk tolerance, a thorough risk assessment may ascertain the most suitable technique for the particular context. The CDC advises that while doffing PPE, it should be removed following a systematic method in the presence of a qualified observer in a designated place to minimize exposure risk. Doffing must occur upon exiting a patient area distinctly segregated from the donning area, ensuring proper placement of a biohazard container. Disposable PPE must be disposed of in a biohazard container after probable exposure to patient tissue or fluids, regardless of visible contamination, and should never be reused. Biohazard containment bins are often positioned near the work area but must be distinct from storage and wearing zones. Necessary cleaning of equipment may be conducted near the doffing zones. An instance would be the decontamination of face shields or safety glasses that have been soiled by a splash from a patient specimen.

8. Conclusion

Clinical labs conduct billions of tests annually, and any deficiencies or lapses in safety protocols at any stage of the testing process might substantially affect laboratory staff, healthcare professionals, patient care, and public health. This review emphasizes the biosafety-related deficiencies and issues that impacted clinical laboratory testing during the 2014 Ebola outbreak, as well as those that continue to affect routine clinical laboratory operations amid the ongoing COVID-19 pandemic and may influence laboratory services during future infectious disease outbreaks. Clinical laboratories require the capability to store, bank, and archive specimens for prospective research and therapeutic applications (e.g., convalescent plasma treatments for Ebola). Many clinical labs, however, are deficient in physical space for safe specimen storage, lack sufficient storage units (including backup systems), and do not possess suitable computerized inventory systems.

Clinical labs are distinct environments, and their vital function in healthcare renders the maintenance and ongoing enhancement of biosafety in these settings' imperative. Individual laboratory risk assessments for the ongoing enhancement of safety procedures, manufacturer initiatives to integrate safety into laboratory equipment design, and systemic efforts by the laboratory community are vital instruments for progress. Laboratory biosafety readiness must be a fundamental element in developing surge capacity to effectively address future outbreaks. This assessment of difficulties, requirements, and objectives in clinical laboratory biosafety aims to facilitate advancements in this field. Additionally, we examined the correlation among biosafety deficiencies, risk assessment, management and mitigation, laboratory safety, and test quality. Despite the efforts of several groups addressing these challenges, no one institution can rectify all existing gaps.

Comprehensive solutions will need the collaborative efforts of laboratory experts and the organizations that assist them. Alongside maintaining laboratory quality, clinical labs must also mitigate hazards to personnel, healthcare institutions, communities, and the environment. Nevertheless, we should not excessively concentrate on addressing the challenges of past outbreaks but rather emphasize the establishment of adaptive mechanisms to enhance laboratory biosafety and develop the ability to more effectively confront the next emerging infectious agent.

References

1. Ngo A, Gandhi P, Miller WG. 2017. Frequency that laboratory tests influence medical decisions. J Appl Lab Med 1:410–414.
2. Beastall GH. 2013. Adding value to laboratory medicine: a professional responsibility. Clin Chem Lab Med 51:221–227.
3. Hallworth MJ. 2011. The '70% claim': what is the evidence base? Ann Clin Biochem 48:487–488.
4. Karwowski MP, Meites E, Fullerton KE, Stroher U, Lowe L, Rayfield M, Blau DM, Knust B, Gindler J, Van Beneden C, Bialek SR, Mead P, Oster AM. Centers for Disease Control and Prevention (CDC). 2014. Clinical inquiries regarding Ebola virus disease received by CDC—United States, July 9-November 15, 2014. MMWR Morb Mortal Wkly Rep 63:1175–1179.
5. Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, Daszak P. 2008. Global trends in emerging infectious diseases. Nature 451:990–993.
6. Castillo-Salgado C. 2010. Trends and directions of global public health surveillance. Epidemiol Rev 32:93–109.
7. Ryan SJ, Carlson CJ, Stewart-Ibarra AM, Borbor-Cordova MJ, Romero MM, Cox SA, Mahon R, Trotman A, St Ville S, Ahmed S. 2017. Outbreak of Zika virus infections, Dominica, 2016. Emerg Infect Dis 23:1926–1927.
8. Clinical Laboratory Improvement Advisory Committee. 2016. Clinical Laboratory Improvement Advisory Committee summary report. Clinical Laboratory Improvement Advisory Committee, Atlanta, GA.
9. Madad S, Spencer C. 2021. The USA's response to the 2014 Ebola outbreak could have informed its COVID-19 response. Lancet 397:965–966.
10. Office of Management and Budget. 1997. Revisions to the standards for the classification of federal data on race and ethnicity. Federal Register 62:36873–36946.

11. Tan KR, Cullen KA, Koumans EH, Arguin PM. 2016. Inadequate diagnosis and treatment of malaria among travelers returning from Africa during the Ebola epidemic—United States, 2014–2015. MMWR Morb Mortal Wkly Rep 65:27–29.
12. Eisler P. 2014. Latest Ebola fear: safety of lab equipment. USA Today.
13. Dubov A, Appleton JH, Campbell S. 2016. Ebola virus preparedness: emerging viruses and ethics in laboratory medicine. Arch Pathol Lab Med 140:171–180.
14. Meechan PJ, Potts J. 2020. Biosafety in microbiological and biomedical laboratories, 6th ed. Department of Health and Human Services, Washington, DC.
15. Miller JM, Astles R, Baszler T, Chapin K, Carey R, Garcia L, Gray L, Larone D, Pentella M, Pollock A, Shapiro DS, Weirich E, Wiedbrauk D. Centers for Disease Control and Prevention (CDC). 2012. Guidelines for safe work practices in human and animal medical diagnostic laboratories. Recommendations of a CDC-convened, Biosafety Blue Ribbon Panel. MMWR Suppl 61:1–102.
16. Troiano A. 2019. Clinical laboratories: using BSL-2 plus when working with pathogens transmitted via inhalation, Environmental Health and Engineering, Inc.
17. Jahrling PB, Keith L, St Claire M, Johnson RF, Bollinger L, Lackemeyer MG, Hensley LE, Kindrachuk J, Kuhn JH. 2014. The NIAID Integrated Research Facility at Frederick, Maryland: a unique international resource to facilitate medical countermeasure development for BSL-4 pathogens. Pathog Dis 71:213–219.
18. Piqueras M. 2007. Microbiology: a dangerous profession? Int Microbiol 10:217–226.
19. Sewell DL. 1995. Laboratory-associated infections and biosafety. Clin Microbiol Rev 8:389–405.
20. Reitman M, Wedum AG. 1956. Microbiological safety. Public Health Rep 71:659–665.
21. Pike RM. 1979. Laboratory-associated infections: incidence, fatalities, causes, and prevention. Annu Rev Microbiol 33:41–66.
22. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. 2018. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 392:1789–1858.
23. Pruss-Ustun A, Rapiti E, Hutin Y. 2005. Estimation of the global burden of disease attributable to contaminated sharps injuries among health-care workers. Am J Ind Med 48:482–490.
24. Baron EJ, Miller JM. 2008. Bacterial and fungal infections among diagnostic laboratory workers: evaluating the risks. Diagn Microbiol Infect Dis 60:241–246.
25. Centers for Disease Control and Prevention Division of Viral Hepatitis. 2018. Viral hepatitis surveillance United States.
26. Egro FM, Nwaiwu CA, Smith S, Harper JD, Spiess AM. 2017. Seroconversion rates among health care workers exposed to hepatitis C virus-contaminated body fluids: the University of Pittsburgh 13-year experience. Am J Infect Control 45:1001–1005.
27. Howerton D, Anderson N, Bosse D, Granade S, Westbrook G. 2005. Good laboratory practices for waived testing sites: survey findings from testing sites holding a certificate of waiver under the clinical laboratory improvement amendments of 1988 and recommendations for promoting quality testing. MMWR Recomm Rep 54:1–25.
28. Centers for Disease Control and Prevention. 1974. Classification of etiologic agents on the basis of hazard. Centers for Disease Control and Prevention, Office of Biosafety, Atlanta, GA.
29. National Cancer Institute. 1975. National Cancer Institute safety standards for research involving oncogenic viruses, NIH 75–790. The National Institutes of Health (US) NCI, Office of Research Safety, DHEW, Bethesda, MD.
30. Wilson DJ. 1993. NIH guidelines for research involving recombinant DNA molecules. Account Res 3:177–185.
31. Hawkes N. 1979. Smallpox death in Britain challenges presumption of laboratory safety. Science 203:855–856.
32. Richmond JY, McKinney RW. Centers for Disease Control (U.S.), National Institutes of Health (U.S.). 1993. Biosafety in microbiological and biomedical laboratories, 3rd ed. U.S. G.P.O., Washington, DC.

33. Joyce MP, Kuhar D, Brooks JT. 2015. Notes from the field: occupationally acquired HIV infection among health care workers—United States, 1985-2013. MMWR Morb Mortal Wkly Rep 63:1245–1246.
34. Bureau of Labor Statistics. 1988. Occupational employment statistics. Bureau of Labor Statistics, Washington, DC.
35. Garner JS. 1996. Guideline for isolation precautions in hospitals. The Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 17:53–80.
36. Lynch P, Jackson MM, Cummings MJ, Stamm WE. 1987. Rethinking the role of isolation practices in the prevention of nosocomial infections. Ann Intern Med 107:243–246.
37. Siegel J, Rhinhart E, Jackson M, Chiarello L, Hospital Infection Control Advisory Committee. 2007. Guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings. Centers for Disease Control and Prevention, Atlanta, GA.
38. Occupational Safety and Health Administration. 1991. Bloodborne pathogens standard. 1910.1030. OSHA, Department of Labor, Washington, DC.
39. Occupational Health and Safety Administration. 2003. Standards interpretation Needlestick Safety and Prevention Act and the requirement to include safety-engineered sharps devices in pre-packaged surgical kits or trays. Department of Labor, OSHA, Washington, DC.
40. US Department of Health and Human Services. 2002. Part IV Title 42 CFR Part 73, Office of the Inspector General, Title 42 CFR Part 1003. Possession, use and transfer of select agents and toxins. Interim Final Rule 67:76886–76905.
41. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, U.S. Department of Agriculture, Animal and Plant Health Inspection Services. 2020. Annual report of the federal Select Agent Program.
42. Soria A, Alteri C, Scarlatti G, Bertoli A, Tolazzi M, Balestra E, Bellocchi MC, Continenza F, Carioti L, Biasin M, Trabattoni D, Bandera A, Ceccherini-Silberstein F, Perno CF, Gori A. 2017. Occupational HIV infection in a research laboratory with unknown mode of transmission: a case report. Clin Infect Dis 64:810–813.
43. Singh K. 2009. Laboratory-acquired infections. Clin Infect Dis 49:142–147.
44. National Academies of Sciences, Engineering, and Medicine. 2018. A smarter national surveillance system for occupational safety and health in the 21st century. The National Academies Press, Washington, DC. 10.17226/24835.
45. American Biological Safety Association International. 2017. Laboratory-acquired infection (LAI) database. ABSA International, Mundelein, IL.
46. Centers for Disease Control and Prevention. 2014. CDC lab incident: anthrax.
47. Grady D, McNeil D. 2014. Ebola sample is mishandled at CDC lab in latest error. New York Times, New York, NY.
48. National Institutes of Health. 2017. Report of the Blue Ribbon Panel to review the 2014 smallpox (Variola) virus incident on the NIH campus. National Institutes of Health, Bethesda, MD.
49. Holdren JP, Monaco L. 18 August 2014. Enhancing biosafety and biosecurity in the United States. The White House, Washington, DC.
50. U.S. Government Accountability Office. 2019. Search for “High Containment Laboratories”.
51. Centers for Disease Control and Prevention. 2018. CLIA law and regulations.
52. Centers for Disease Control and Prevention. 2019. The laboratory response network partners in preparedness.
53. Association of Public Health Laboratories. 2018. Strengthening lab biosafety & biosecurity.
54. Munson E, Bowles EJ, Dern R, Beck E, Podzorski RP, Bateman AC, Block TK, Kropp JL, Radke T, Siebers K, Simmons B, Smith MA, Spray-Larson F, Warshauer DM. 2017. Laboratory focus on improving the culture of biosafety: statewide risk assessment of clinical laboratories that process specimens for microbiologic analysis. J Clin Microbiol 56:e01569-17.
55. Centers for Medicare and Medicaid Services. 2019. Clinical laboratory improvement amendments (CLIA).

56. Centers for Medicare and Medicaid Services. 2005. 42 CFR 493 - Laboratory Requirements. 42 - Public Health. 42 U.S.C. 1302, 1395x and 263a.
57. Centers for Medicare and Medicaid Services. 2017. State operations manual appendix C—survey procedures and interpretive guidelines for laboratories and laboratory services. U.S. Department of Health and Human Services, Washington, DC.
58. College of American Pathologists. 2017. Accreditation checklists. www.cap.org/laboratory-improvement/accreditation/accreditation-checklists?_adf.ctrl-state=a3u45376f_4.
59. The Joint Commission. 2019. Comprehensive accreditation manual for laboratory and point-of-care testing. Joint Commission Resources, Oak Brook, IL.
60. Wilson ML, Gradus S, Zimmerman SJ. 2010. The role of local public health laboratories. Public Health Rep 125 Suppl 2:118–122.
61. Plebani M. 2012. Quality indicators to detect pre-analytical errors in laboratory testing. Clin Biochem Rev 33:85–88.
62. The Joint Commission. 2002. Joint Commission national patient safety goals; NPSG.7.01.01, NPSG.07.03.01. Joint Commission Resources, Oakbrook Terrace, IL.
63. Centers for Disease Control and Prevention. 2019. Type and duration of precautions recommended for selected infections and conditions. https://www.cdc.gov/infectioncontrol/guidelines/isolation/appendix/type-duration-precautions.html.
64. Centers for Disease Control and Prevention. 2017. Standard precautions for all patient care.
65. Foote M, Daver R, Quinn C. 2017. Using "mystery patient" drills to assess hospital Ebola preparedness in New York City, 2014–2015. Health Secur 15:500–508.
66. Foote M, Styles TS, Quinn CL. 2017. Assessment of hospital emergency department response to potentially infectious diseases using unannounced mystery patient drills—New York City, 2016. MMWR Morb Mortal Wkly Rep 66:945–949. 10.15585/mmwr.mm6636a2.
67. Song J, Zhou W, Wang Y, Cui Y, Huang XX, Zhang BY, Wu GZ, Han J, Dong XP. 2012. Contamination of live virus during tissue homogenizing by ultrasonic processor and tissue disperser. Biomed Environ Sci 25:167–171.
68. Wang XL, Song J, Song QQ, Yu J, Luo XN, Wu GZ, Han J. 2016. Viral contamination source in clinical microbiology laboratory. Biomed Environ Sci 29:609–611.
69. Yarbrough ML, Kwon JH, Wallace MA, Hink T, Shupe A, Fraser VJ, Dubberke ER, Burnham CA. 2018. Frequency of instrument, environment, and laboratory technologist contamination during routine diagnostic testing of infectious specimens. J Clin Microbiol 56:225–218.
70. Jaeger JL, Patel M, Dharan N, Hancock K, Meites E, Mattson C, Gladden M, Sugerman D, Doshi S, Blau D, Harriman K, Whaley M, Sun H, Ginsberg M, Kao AS, Kriner P, Lindstrom S, Jain S, Katz J, Finelli L, Olsen SJ, Kallen AJ. 2011. Transmission of 2009 pandemic influenza A (H1N1) virus among healthcare personnel—Southern California, 2009. Infect Control Hosp Epidemiol 32:1149–1157.
71. Centers for Disease Control and Prevention. 2015. Guidance on personal protective equipment (PPE) to be used by healthcare workers during management of patients with confirmed Ebola or persons under investigation (PUIs) for Ebola who are clinically unstable or have bleeding, vomiting, or diarrhea in U.S. hospitals, including procedures for donning and doffing PPE.
72. Cornish, N.E., Anderson, N.L., Arambula, D.G., Arduino, M.J., Bryan, A., Burton, N.C., Chen, B., Dickson, B.A., Giri, J.G., Griffith, N.K. and Pentella, M.A., 2021. Clinical laboratory biosafety gaps: lessons learned from past outbreaks reveal a path to a safer future. Clinical microbiology reviews, 34(3), pp.10-1128.
73. Mukadi-Bamuleka, D., Mambu-Mbika, F., De Weggheleire, A., Edidi-Atani, F., Bulabula-Penge, J., Mfumu, M.M.K., Legand, A., Nkuba-Ndaye, A., N'kasar, Y.T.T., Mbala-Kingebeni, P. and Klena, J.D., 2023. Efficiency of field laboratories for Ebola virus disease outbreak during chronic insecurity, eastern Democratic Republic of the Congo, 2018–2020. Emerging Infectious Diseases, 29(1).

الملخص

الخلفية :تعد المختبرات السريرية ضرورية لرعاية المرضى والصحة العامة، لا سيما أثناء تفشي الأمراض المعدية. أظهرت فاشية الإيبولا عام 2014 أوجه قصور كبيرة في بروتوكولات السلامة البيولوجية داخل المختبرات السريرية، مما أثر سلبًا على نتائج المرضى. تستكشف هذه الدراسة التحديات والحالة الحالية للسلامة البيولوجية وإدارة المخاطر في المختبرات السريرية، لا سيما في ضوء الأوبئة الحديثة.

الطرق :تم إجراء مراجعة شاملة للأدبيات والإرشادات المتعلقة بالسلامة البيولوجية في المختبرات، مع التركيز على الحوادث أثناء تفشي الإيبولا وكوفيد-19. شملت التحليل الأطر التنظيمية والبروتوكولات الحالية للسلامة البيولوجية ودراسات الحالة التي توضح أوجه القصور في تدابير السلامة.

النتائج :أشارت النتائج إلى أن العديد من المختبرات السريرية تعمل تحت إشراف تنظيمي محدود، خاصة تلك الحاصلة على شهادة CLIA للإعفاء. تم تحديد نقص في ممارسات السلامة البيولوجية الموحدة، مما أدى إلى زيادة مخاطر العدوى المكتسبة داخل المختبر. كما كشفت المراجعة أن المختبرات الصحية العامة، رغم أنها مجهزة بشكل أفضل، لا تزال تواجه تحديات في الحفاظ على معايير السلامة البيولوجية بسبب قيود الموارد والظهور السريع لعوامل معدية جديدة.

الخلاصة :تؤكد الدراسة على الحاجة الملحة لتعزيز بروتوكولات السلامة البيولوجية والأطر التنظيمية في المختبرات السريرية للحد من المخاطر المرتبطة بالأمراض المعدية الناشئة. تعد الجهود التعاونية بين العاملين في مجال الرعاية الصحية والهيئات التنظيمية وخبراء المختبرات ضرورية لتطوير استراتيجيات شاملة تضمن سلامة العاملين في المختبرات وموثوقية الفحوصات التشخيصية.

الكلمات المفتاحية :المختبرات السريرية، السلامة البيولوجية، الأمراض المعدية، الأطر التنظيمية، العدوى المكتسبة داخل المختبر.