**CLINICAL RESEARCH INFORMATICS**

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**ABSTRACT**

Clinical research informatics is currently an evolving sub-domain of biomedical informatics that involves the use of informatics in the discovery and application of new knowledge relating to health and diseases and better treatment strategies. It includes the management of processing information in respect to human system integration with machine and data. In other words, all biomedical informatics involved with clinical research is called clinical research informatics. Clinical research informatics (CRI) has recently emerged as an important domain of transition and also in supporting clinical trials, which are often a complex and highly resource intensive process. In the last few years, it has gained the attention of the government, academic, and private sectors, as they have a significant interest in the scientific and financial aspect in the conduct and outcomes of clinical research trials. Clinical researchers face significant challenges in conducting the clinical research trials, as there is a complex workflow process, gathering information management requirements, data storage, and ethical issues. The access to adequate and efficacious information is important to solve the hurdles faced in clinical research trials, therefore, an expeditious transformation of biomedical informatics tools and technologies is the need of the hour and hence clinical research informatics are specifically designed to address the clinical research information management requirements and should be technologically upgraded with time.

**Keywords –** Informatics, biomedical informatics, clinical research, translational research, clinical research informatics.

1. **INTRODUCTION**

Clinical research plays a significant role in the generation of evidence and provides information that can in turn facilitate and improve the quality of the human health with authentic research. However, the management of constructive plan, implementation and evaluation of clinical research is an inherently complex process. It includes intelligence and extensive resource endeavour which includes stakeholders, workflows, processes, data types, data storage, and computational resources [1].

Clinical informatics is the study of application of information technology and informatics to deliver healthcare services. It is also referred to as health informatics or applied clinical informatics [2]. Currently many researchers have absolute focused on increasing their research in the biomedical sector and to bring attention of the stakeholders like government, academician and private sectors and those who have interest in scientific and financial aspect towards clinical research and related biomedical informatics activities or in the outcome of clinical trials [3-10]. These scientific activities and initiatives have increased in significant emergence of a new sub-domain in biomedical informatics focused mainly on clinical research, known as the Clinical Research Informatics (CRI). Clinical Research Informatics involves the use of informatics in the discovery and management of new knowledge relating to health and disease. It also involves the managing of clinical research information and deals with the secondary use of clinical trials/ research data. CRI field is growing at a rapid pace and has already brought significant improvements in the quality and efficiency of clinical research and trials [7,11,12]. With the increase interest of clinical researchers in CRI, it is an emerging and promising field of activity and possibility in future. With its evolution, this sub-domain also faces critical challenges and opportunities. To solve these challenges, access to effective and efficient information is important, therefore, there has been a rapid evolution of biomedical informatics tools and technologies specifically designed to address the clinical research information management requirements. Clinical research is itself in a transition state. Clinical research informatics and translational bioinformatics are the primary domains related to informatics activities to support translational research [12].

1. **CLINICAL RESEARCH INFORMATICS**
2. **Informatics**:

Informatics is the study of the structure, operation and interactions of any system that creates, saves, processes, retrieves and analyse data and then presents information. It is the science of how to use information and data to improve human health and healthcare system. It explores the uses of digital technology and information-driven technology, particularly with respect to human systems integration.

1. **Biomedical informatics**:

Biomedical informatics in health sector involves application of information science towards enhancement of the study of life sciences, medical professional and healthcare provider education, patient care and public health redressal. It aims at application of medical information technologies with the use of computer applications along with cognitive and social aspects. Medical information technology permits advancement in healthcare system by providing the methods and tools to set the knowledge in practical applications and practices. The definition of biomedical informatics adopted by the American Medical Informatics Association (AMIA) is ‘the interdisciplinary field that studies and pursues the effective uses of biomedical data, information, and knowledge for scientific inquiry, problem solving and decision making, motivated by efforts to improve human health’[13]. Sub-disciplines of biomedical informatics are: translational informatics, clinical research informatics, and public health informatics.

1. **Clinical research**:

Clinical research plays an important role in the upliftment of medical science, patient care and public health. Clinical trials deal with developing new drugs, devices or procedures which helps in improving human health. Conducting a clinical trial is a complicated process, and has many challenges. It requires funding, and intensive resource centric endeavour, comprising of a complex process and workflows that includes many multidisciplinary experts and information resources [2]. In the last few years, the efforts required in such processes on a large scale to improve the clinical study of biomedical sector have been able to bring the attention of government, private sectors, academicians, and non profit organizations on the activities of biomedical informatics and biomedical research [3-10]. The emergence of Clinical Research Informatics (CRI), which is a sub-domain of biomedical informatics constantly focuses on biomedical research activities. There has been a rapid and significant improvement in the efficiency and standard of clinical research in the last 5-10 years [7, 11]. According to the National Institute of Health (NIH) (1997), Clinical research involves, “the range of studies and trials in human subjects that fall into the three sub-categories: (1) Patient-oriented research: Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. Patient-oriented research includes: (a) mechanisms of human disease; (b) therapeutic interventions; (c) clinical trials, and (d) development of new technologies. (2) Epidemiologic and behavioural studies. (3) Outcomes research and health services research” [14,15].

1. **Clinical research informatics (CRI):**

Embi and Payne, 2009, defined Clinical Research Informatics as the sub-domain of biomedical informatics concerned with the development, evaluation and application of informatics theory, methods and systems to improve the design and conduct of clinical research and to disseminate the knowledge gained [1]. Clinical research informatics also includes retrospective studies and prospective clinical trials. In such kind of studies, CRI aims for the evolution of systems and tools supporting the researchers to enlighten the research methodology with previously collected data or to collect new research data in their own studies. The major area of focus of CRI is clinical data archives and data management methodology for clinical experiment [16].

With the evolution and rapid progress of Clinical research informatics (CRI), there is an astounding rise in opportunity and momentum of clinical and translational (bench to bedside) research, which has brought attention of major funding programs such as that of National Institute of Health’s (NIH) Road map initiative, department of biotechnology research programs, Indian council of medical research programs and establishment of medical and research wing in different medical colleges [17]. One of the crucial goals of the NIH Road map are schemes to fundamentally reform the way in which organizations and researchers transcribe basic science recognition into practical therapeutics [6,17,18]. Clinical and Translational Science Award (CTSA) is among one of such program which is intended to rebuild the way in which academic health research centres manage and fund clinical trial and translational science [5, 6,19]. Indian council of medical research (ICMR) awards also boosts researchers to carry out quality research in different fields of medical science and public health. These platforms are to systematize and expand a variety of CRI-based programs that includes data warehousing, clinical research management and manpower recruitment systems, cooperative team science tools, and integrative data streamlining and acceptable harmonization platforms [19]. Like CTSA program, there are many other significant programs that represent CRI domain activities. Few examples include:(1) the NCI’s Cancer Biomedical Informatics Grid (caBIG) initiative [3,4,7,8] (2) Various CRI focused standards and harmonization bodies such as the Clinical Data Interchange Standards Consortium (CDISC), Health Level 7 (HL7), and the Biomedical Research Integrated Domain Group (BRIDG) [20-23]; (3) The creation and growth of clinical trial data registries; [24-26] and (4) other NIH Road map initiatives such as the “re-engineering the clinical research enterprise” program which preceded the CTSA initiative and spawned the fundamental workflow and information management needs of the clinical research domain [17,27,28,29]. Additionally, in the last decade there has been an emergence of literatures explaining the challenges to the national clinical research sector and the coordinated benefits that would result from addressing these challenges thoroughly, or in fragments, or with effective integration of biomedical informatics with translational research workflows [5,8,11].

1. **Translational research**:

National Institute of Health (NIH) defines Translational research, as covering two areas of translation: one is the process of applying discoveries generated during research in the laboratory, and in preclinical studies, to the development of trials and studies in humans. The second area of translation concerns research aimed at enhancing the adoption of best practices in the community. Cost-effectiveness of prevention and treatment strategies is also an important part of translational science [30]. One of the example of translational research is study of cancer therapy where an extensive collaborative dedicated team is required that comprises of basic researchers, clinicians and industry, that follows a discovery of a new targeted compound/ drug with better efficacy and less toxicity. Translational research acts as a bridge between the various areas of research, connecting their outcomes to each other, and ultimately its benefit to the community at large.

1. **APPLICATION OF INFORMATICS IN RESEARCH**

Clinical research involves a variety of knowledge sources along with collection of variety of data and information and is a complex set of complementary and overlapping workflows modules. Clinical research environment requires a number of critical informational needs. Clinical research methodology traverses through the spectrum from observational studies to interventional trials. It may be as simple as administering a substance that is already found inside a human body and observing its change in the body (such as the amount of vitamin found in blood or urine), or it can be a more complex interventional studies like administration of a preventive vaccine e.g., emergence of covid vaccine during Covid 19 pandemic.

Data collection is critical in passive or observational studies for the proper performance of research. In interventional trials/ studies, it may become more complex with the compilation of clinical information that occurs more frequently which involves data describing the intervention materials (example effectiveness of a drug) and data related of study subject and their response to the clinical trial. Clinical study endeavours existence on a spectrum of scientific activities commonly referred to as the clinical and translational research. Translational research involves a series of processes with the help of which basic science discoveries are used to design novel drug therapies and procedure. These discoveries are then evaluated through a series of clinical trials phases 1-4, first in pre-clinical phase and subsequently in clinical trial phases [7]. Data coordinating centres can provide support for researchers to gain access to various study designs, research questions, data sources, patient and disease domains in clinical research.

1. **CHALLENGES AND ETHICAL ISSUES OF CRI**

Clinical researchers face significant challenges in conducting the clinical research trials. To conduct a clinical research trial, sufficient information tools and technologies, infrastructure and apps are required. The need for a reliance on workflows defined by historical precedence rather than optimal operational strategies, account for hindrance to the convenient, effective, and resource efficient conduct of clinical research activities and trails [7]. The swift enhancement of biomedical research and the need for the upgradation in healthcare system demands that the clinical research should be timely, efficiently, and should yield high quality results of public importance and service [31,32]. This has led to significant requirement of clinical care data available and easily accessible for the secondary use in support of clinical research and has become an urgent need for clinical and research methodology [32,33]. Moreover, the increasing sophistication of medical research in association with challenges to cope with the regulatory requirements during clinical studies have created further changes in the clinical research, that includes a trend towards conducting clinical trials in community practice, which is completely opposite than earlier norms of conducting such studies in large Academic Health Centers (AHCs) [27,32]. This rapid growth and expansion of clinical research field has led the stakeholders in the clinical research environment to acknowledge the upcoming situation and call for system-level solutions [15,32].

Clinical research in itself is in a transition phase and it faces critical challenges in information management requirements. With the evolution of clinical research field in a large scale, it has gained attention of government, public sectors and academicians, who have interest in scientific and economical interest in conducting research, clinical trials and management, and its outcome. With an increase interest of researchers in this domain, the timely access to the data and information, that is effective and efficient to find the solution of the challenges faced is critical. It demands transparent research, data sharing and standardized methods that can be easily replicated. Therefore, this has led to rapid evolution in biomedical informatics to develop tools and technologies, designed to fulfilment of clinical research and logistic support [12]. New application and tools for CRI systems have been developed in order to enable real-world evidence based medicine and optimize the lifecycle of clinical trials [34].

Ethical and public redressal are major issues in biomedical and clinical research. There is a growing interest in the ethical related issues of health informatics research and innovation. The complexity of regulatory guidelines and variation between different regulatory bodies is a matter of concern in this field. The development of designing tool and technologies using artificial intelligence has gained maximum attention at present in all the scientific and research fields. There should be uniformity in following the ethical principles worldwide to maintain a uniform standard in the research field in order to boost the confidence of the researchers themselves and to guide others to follow ethical principles correctly. Many nations including India are publishing principles and guidelines of ethical issues, or enactment via legislation (like the European AI Act) [35]. Data breach and protecting patient privacy and data confidentiality is still a significant threat. Uniform standard and robust guidelines should be strictly prepared and followed to protect the patient privacy and data confidentiality, which also requires an advanced network security safeguards. [36]

1. **FUTURE ASPECT OF CRI**

Clinical Research Informatics is an emerging and evolving sub-domain, with increase in availability of literatures in various CRI topics such as data collection, information processing, designing methods and tools, planning management, and data analysis. In future, researchers may develop more interesting tools and technologies which are effective for clinical trials and translational research that is more patient oriented and beneficial for a healthy lifestyle for human. Use of artificial intelligence may be encouraged in developing the tools and technologies and to make it easily accessible for the other researchers. The most significant research efforts in CRI in current scenario are focused on their research on data science and technology with interest in the evolution and development of artificial intelligence algorithms based on intensive use of real world information and technology. Timely sharing of high-end information and collaborative data analysis is very vital to a good research and subsequently inform policy decisions [37].

In future, CRI is expected to enhance clinical research methodologies, facilitate and will generate real time evidence based research that can bring fundamental change in the time, direction, effectiveness and worthiness of the clinical research enterprise and discovery. Through CRI, biomedical advances, clinical trials, discovery, health care quality improvement, development of application informatics and the evidence based medicinal research will become easier [1].

1. **CONCLUSION**

Clinical research informatics (CRI) is emerging as an important sub-domain of biomedical informatics, and is one which is still nurturing and altogether facing many challenges and generating opportunities. Clinical research unit is fundamental to the generation of evidence based research that can facilitate upliftment in the quality of human well being and diseases. Data coordinating centers must have the facility of the clinical research informatics, frameworks and tools to support a wide variety of study designs, research questions, various domains for disease and patient populations, and data sources in clinical research. Framing various study design and implementation models for clinical research/ trials faces many challenges, especially for identifying the optimal standards for medication data. In the CRI field, most significant efforts are made on research data science along with the development and proper utilisation of Artificial Intelligence (AI) algorithms based on comprehensive use of real time world database. Collaborative effort of data collection, data-sharing, editing and data analysis worldwide is significantly important to enroll policy decisions.

The clinical research field is rapidly progressing and altogether facing challenges in significant manpower and information management. In recent years, the government, academic, private-sectors and funding agencies has shown their interest in clinical research and more importance in the efforts of the outcome of clinical study/ trials. This rapid advent explains emergence of clinical research informatics as a very important and esteemed part of biomedical informatics. The evolution of CRI can be credited to the exemplary rise in the scope and pace of basic science, clinical and translational science clinical trial, research and developmental activities that has been supported by a variety of funding and policy initiatives that has helped to restructure the way in which government, public, and private sectors ideology and take active part in the advancement of the basic science discoveries into practical therapeutics. CRI in due course of time has emerged as an effective and cognate sub-domain of biomedical informatics, which provides a broad spectrum of research and development opportunities and possibilities in context to both basic and applied medical informatics.

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