CLINICAL RESEARCH INFORMATICS

Abstract

Clinical research informatics is a 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. With its evolution, in the last few years, the various organizations like the government, academic, and private sectors have showed their interest in the scientific and financial aspect in the conduct and outcomes of clinical research trials. Clinical researchers have been facing significant challenges in conducting the clinical research trials, as it involves a complex workflow process, like gathering information management requirements, data storage, accessibility, reliability, and ethical issues. The easy access to adequate and efficacious high-quality, reliable data information is important to solve the hurdles faced in clinical trials; therefore, an expeditious transformation of biomedical informatics tools and technologies is the need of the hour. Hence, clinical research informatics should specifically designed advanced tools and methods to address the clinical research information management requirements and it should be technologically upgraded with time. Uniform standard and robust guidelines should be prepared to protect patient privacy and confidentiality of data, with an

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advanced network security safeguard system.

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I. 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 interested on increasing their research in the biomedical sector has caught the attention of the organizations 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 led to an emergence of a new sub-domain in biomedical informatics focused mainly on clinical research, known as the Clinical Research Informatics (CRI). CRI involves the utilization of information processes and the engineering of information systems in the discovery and management of new skills and information relating to health, well being and diseases. It also includes the managing of clinical research information and deals with the secondary use of clinical trials/ research data. In all kind of research work, data is the main building block, based on which analysis and conclusions are formed. CRI main goal is to provide statistically sound, high quality, reliable data, but the challenge is to assess the quality of the data, enormous data storage, and their intended use [11,12,13,14] Poor clinical informatics data quality may affect adversely the quality of the research outcomes, healthcare services and in healthcare policy-making. [15] The CRI field is growing at a rapid pace and it has already brought significant improvements in the quality and efficiency of clinical research and trials [2,7,16]. 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 specifically designing the biomedical informatics tools and technologies to address the clinical research information management requirements. Clinical research is itself in a transition state. Clinical research informatics and translational bioinformatics are the two primary subject area related to information studies and activities to support translational research[2].

II. CLINICAL RESEARCH INFORMATICS

1. **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.

2. **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 science that educates and follows the efficacious use of bioscientific information for scientific enquiry, problem based solution and decision making, motivated by efforts to ameliorate public health and diseases'[17]. Sub-disciplines of biomedical informatics are: translational informatics, clinical research informatics, and public health informatics.

3. **Clinical Research:** Clinical research plays an important role in the upliftment of bio-medical science, patient care and public health. Clinical trials deal with developing new drugs, devices or procedures which helps in improving human health, and its integration with informatics plays a significant role in improving drug discovery, patient care and redefining the traditional trial processes. As the integration with informatics propels clinical trials into data-driven era, certain issues need to be considered and strictly regulated like ethics, patient consent, data privacy, which is the responsibility of all the stakeholders: researchers, clinicians, regulatory bodies, sponsoring and information technology organizations, etc. [18]. 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 [7,16]. According to the National Institute of Health (NIH) (1997), Clinical research involves, "the scope of studies and experiments in subjected population that falls under these three classification: (1) Patient-oriented research: Research conducted with patient subjects (or on a subject matter of human origin such as tissues, specimens and cognitive phenomena) which involves a principal investigator (or colleague) to directly interact with human subjects. Patient-oriented research includes: (a) Anatomical, physiological, biochemical and pathological changes and mechanisms of human disease (b) research that involves therapeutic interventions; (c) clinical trial oriented research, and (d) development of newer technology. (2) Behavioural and Epidemiologic studies. (3) Outcomes oriented research and health services research"[19,20].

4. **Clinical Research Informatics (CRI):** Clinical Research Informatics is the sub-class of biomedical informatics concerned with the progress, assessment, evaluation and application of informatics knowledge, materials and methods and system techniques to improve the blueprint of study design and conduct clinical research and to disseminate the knowledge gained for the alleviation of disease and upliftment of health of the people [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 [21]. Application of tools and technologies of CRI like electronic medical records (EMRs), patient portals, smartphone healthcare apps, telehealth, and many more data reporting tools are available to deliver healthcare services. [22].

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[23]. 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 [6,23,24]. 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 [5,6,25]. 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, integrative data streamlining and acceptable harmonization platforms [25]. Like CTSA program, there are many other significant programs that represent CRI domain activities. Few examples include:(1) The US National Cancer Institutes Cancer Biomedical Informatics Grid (caBIG) initiative [3,4,7,8] (2) 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) [26-29]; (3) The creation and growth of clinical trial data registries; [30-32] and (4) NIH Road map initiatives such as the "re-engineering the clinical research enterprise" program which preceded the CTSA initiative and generated the basic workflow and information asset management needs of the clinical research fundamentals [23,33,34,35]. (5) National cancer registry program, India with 38 population based cancer registry and 189 hospital based cancer registry [36]. Additionally, in the last decade there has been an emergence of literatures explaining the challenges to the national clinical research field and the coordinated benefits in addressing these challenges thoroughly, or in fragments, or effective with integration of biomedical informatics and translational research workflows [5,8,16].

5. **Translational Research:** According to National Institute of Health (NIH), Translational research covers two areas of translation: (1) The process of applying discoveries generated during research in the laboratory, and in preclinical research, to the development of trials and studies in humans. (2) Translation is aimed at enhancement and the adoption of best practices in the community. An important part of translational science is development of cost-effective prevention, treatment and management strategies [37]. An example of translational research is the study of cancer therapy where an extensive collaborative dedicated team is required that comprises of basic researchers, clinicians, surgeons 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.

III. 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 scope from observational research to interventional trials. It may vary from a simple study such as administering a substance that is already present in a human body and observing its change in the body (like the amount of vitamin found in blood or urine), to a more complex interventional studies like immunization with a 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 due to compilation of clinical data that occurs more frequently which involves data that describes the interventional materials, logistics (example effectiveness of a drug) and data related to study subject and their behaviour to the clinical trial and effectiveness of the therapy. Clinical research endeavours existence on a variety of scientific activities often been referred to as the clinical and translational research. Translational research involves a series of processes with the help of which discoveries of basic science are applied to design novel drug therapies and procedure. These explorations 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, and patient and disease domains in clinical research.

IV. CHALLENGES AND ETHICAL ISSUES

Clinical researchers face significant challenges in conducting the clinical research trials. To conduct a clinical research trial, sufficient information of tools and technologies, infrastructure and apps are required. The need for streamlined workflows of study defined by historical supersede rather than outstanding operational strategies may account for hindrance to the convenient, easier, effective, and resource efficient regulation of clinical research trials and activity [7]. The swift enhancement of bioscience research and the requirement for the upgradation in healthcare system demands that the clinical study should yield excellent results and outcome of public importance and service [6,38]. This has led to significant requirement of healthcare information data availability and easy accessibility for the consequent use in support of healthcare investigation and research and has enhanced an urgent need for healthcare, clinical and research methodology [38,39]. In addition to this, the increasing sophistication of medical investigation in association with challenges to cope with the regulatory requirements during clinical studies have created further changes in the clinical and medicolegal research, that includes an inclination towards clinical trials in community, which is completely opposite than earlier norms of organizing such studies in hospitals and medical colleges [33,38]. This rapid growth and expansion in the field of clinical research has led the collaborators in the clinical research ecosystem to recognize the upcoming situation and call for government, private and collaborative system-level solutions [20,38].

Clinical research in itself is in an evolutionary 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 [2]. New application and tools for CRI systems have been designed and developed conducive to authorize authentic and updated evidence based medicine and refine the continuance of clinical trials [40].

Ethical and public redressed are the major issues in biomedical and clinical research. There is a growing interest in the ethical related issues of bio health specific information 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. Artificial intelligence (AI) and machine learning (ML) are technologies that are extensively used in CRI for increased availability and processing of clinical data in digital forum. [41]. However, there are also potential risks in extensive use of AI algorithm in its implications for patients' treatment and healthcare delivery. [42]. 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) [43]. 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 confidentiality of data, which also demands an advanced network security safeguard system that should be assessed for any breach time to time [44]. Maintaining of data and providing high quality and reliable data is very important task of CRI. Assessing and improving the quality of data used by CRI tools are equally important and difficult tasks. A high data quality translates into better research outcome which may apply to better patient health care. However, the challenge is in achieving and creating standards for high-quality data, as there are many ways of generating errors and difficulty in correcting them in the system. [16].

V. THE WAY FORWARD

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 noteworthy research endeavour 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 blueprint based on accelerated use of genuine world information and technology. Timely sharing of high-end information and combined evidence based data analysis is of utmost importance to a good research and subsequently inform policy decisions [45].

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 organization and discovery. Through CRI, biomedical engineering advances, clinical trials, quality health care, development of application informatics and the evidence based medicinal research will become easier [1]. Looking forward, CRI can enhance and promote health equity with specifically designed newer digital tools and technologies with ethical considerations and patient data privacy and confidentiality.

VI. 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 the basic principle to the propagation of evidence and documentation 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 enrol in the decision making policy.

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 progression of CRI can be credited to the exemplary rise in the basic science possibilities, clinical and translational science clinical trial, research and developmental activities supported by a variety of sponsors and policy makers initiatives that has helped to restructure the approach in which government, public, and private sectors ideology and take active part in the advancement of the basic science revelations into practical therapeutics. CRI in due course of time has emerged as an effective and cognate sub-domain of biomedical informatics, which provides an all round research and development probabilities in context to both basic and applied medical informatics.

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