



CLINICAL RESEARCH IN PAKISTAN: PAST, PRESENT AND FUTURE PROSPECTS

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Pakistan is the 5th most populous country in the world with a population of 229.5 million in 2022.¹ Like any developing country, Pakistan is facing various health-related challenges with a huge burden of communicable and non-communicable diseases, poor indicators of maternal and newborn health, nutrition and life expectancy.^{2,3} Pakistan has a unique population with diverse genetic, lifestyle, socioeconomic, cultural and environmental factors that can affect the disease burden, progression, and response to treatment. Local clinical research is required to understand these factors and develop healthcare interventions tailored to the needs of the Pakistani population. This targeted approach will not only be helpful in addressing the local problems but will have a regional and global impact, especially for other developing countries.

First documented evidence of clinical trials from Pakistan, available on PubMed can be traced back to 1963-1964, when Cholera vaccine field trials were conducted in East Pakistan.^{4,5} Pubmed search revealed that four clinical trials were published in 1968, forty trials were published from 1969-1990, 152 trials were published from 1991-2000, 403 from 2001-2010 and 2737 trials were published from 2011 till February 2023.⁶

Clinical trials registration with any one of the primary registries by World Health Organization (WHO), International Clinical Trials Registry Platform (ICTRP)⁷ is required by for publication of all clinical trials.⁸ Unfortunately, clinical trials registration is not done for all trials being conducted in Pakistan. However, data of

clinicaltrials.gov showed 2231 clinical trials registered from Pakistan till March 01, 2023; 1895 were Interventional studies, 1471 studies were completed studies, 395 were recruiting, 61 studies were active-not recruiting studies and 66 studies were not-yet recruiting studies.⁹ Clinical trials from Pakistan registered with Iranian Registry of Clinical Trials (IRCT) and Australian New Zealand Clinical Trials Registry (CTR) till March 01, 2023, were 355 and 164 respectively.^{10,11}

Although the only local CTR of Drug Regulatory Authority of Pakistan (DRAP) is still not included in the list of primary registries by WHO ICTRP. DRAP website shows only 36 clinical trials registered with CTR of DRAP (list of approved clinical trials and studies, updated on DRAP website is till 30th May, 2022).¹²

Evidence is suggestive of an increasing trend in the number of clinical trials registered from Pakistan.¹³ However, despite of having a large population, sharing a significant pool of patients and rapidly growing pharmaceutical market, Pakistan sharing only 0.1% of the global clinical trials, is not comparable to its real capability.¹⁴ Main factors that may impede the output of clinical trials in Pakistan, like other developing countries include inadequate infrastructure, insufficient resources, limited trained and skilled researchers, lack of funding, lack of effective collaboration, poor quality assurance and regulatory barriers.¹⁵

Pakistan faces a shortage of research infrastructure, required to conduct of the clinical trials in a safe, effective, and efficient manner. Currently well-equipped laboratories and advanced research facilities are only available in

major tertiary care hospitals, medical universities and other research institutes. DRAP requires mandatory approval of Clinical Trial Site(s) (CTS) for conducting clinical trials in Pakistan.¹⁶ As per available information on DRAP website, total 82 CTS (49 trial specific & 33 Generalized) are approved by DRAP (List of approved CTS updated till 30th May, 2022). Out of 82 CTS, 34 were from Punjab, 33 from Sindh, 7 from Islamabad and 4 each from Khyber Pakhtunkhwa and Balochistan.¹⁷ Majority of centers are lacking important resources like clinical trial management systems, data management & analysis, electronic medical record, electronic source document verification and internet connectivity etc.¹⁸

Limited trained and skilled researchers and shortage of qualified research assistants and support staff is another important challenge faced by Pakistan. According to WHO, Pakistan has 5,185 full time equivalent health researchers, 7% of all researchers from WHO Eastern Mediterranean region.¹⁹ Similarly, lack of funding for health research has negative effects on magnitude, quality and scope of clinical research in Pakistan. According to the latest report of World Research and Innovation Transformation (World RePORT), low-income countries received about 0.2% of the annual grant amount. Pakistan received 17.6 Million USD (9.39% of 188 countries) as compared to 38.57 Million USD by India.²⁰ Researchers are spending out of pocket money to conduct doctorate level research in Pakistan. Unfortunately, there is no FDA approved pharmaceutical company in

Pakistan that can invest in clinical research and conduct multi-center clinical trials.¹⁸

Poor quality assurance in clinical trials is another major impediment to the progress of clinical research. Issues related to research ethics committees, poor adherence to study protocol and nonexistence of research integrity offices in universities/research institutions lead to uncertainty about the credibility and trustworthiness of research process and deter international collaboration.

DRAP is doing excellent job in regulating clinical research and safeguarding the rights of research participants. However, certain policies of DRAP create additional obstacles for national and international collaboration in clinical research. Main barriers include mandatory approval of all clinical trials from national bioethics committee, lengthy approval processes complicated with inordinate delays, unclear regulatory requirements, and limited resources to enforce regulations.^{14,16}

Despite of all these challenges and concerns, the future of clinical research in Pakistan is quite promising. Establishment of dedicated clinical trials units at the major research institute and universities in Pakistan is the major development in this regards.¹⁸ Master's in Bioethics is a great step taken by Center of Biomedical Ethics & Culture, Karachi Pakistan.²¹ International Conference on Harmonization- Good Clinical Practice (ICH-GCP) are also being offered by universities and research institutes to the investigators of clinical trials. Medical universities may boost the efforts of producing more skilled researchers by starting Master programs in clinical research.

An important contribution is being extended by Association of Pakistani Physicians of North America (APPNA) in the form of APPNA- Medical Education, Research, International training and transfer of Technology (MERIT).²² APPNA MERIT provides learning opportunities for medical professionals and students in Pakistan, on the latest developments in medical research and practice through weekly webinars by leading experts in the field.

APPNA MERIT has recently taken a great initiative bringing together all key stakeholders from Pakistan, United States and Canada to establish a strong network for strengthening clinical research in Pakistan. They held their first round table national consultation for evolving participatory clinical research ecosystem in Pakistan on Saturday 18th February 2023. Hopefully, a local (Pakistan) chapter of Association of Clinical Research Professionals (ACRP) will be established soon to provide networking and training support to clinical researchers from Pakistan.

Funding is a grave concern, especially during the current financial crises in Pakistan, resulting in a major cut in research grants to higher education institutions. Multifaceted approach is needed to look for national and international funding bodies, government & private non-profit organizations, agencies, foundations and pharmaceutical companies that can provide grants or funding for clinical research in Pakistan, addressing the priority issues of our local population. Researchers should explore potential collaborations with pharma industry and international researchers who are interested in outsourcing of clinical trials in developing countries. To attract international trials, we need to train our researchers, simplify regulatory approval, strengthen our pharmacovigilance system, and ensure strong ethical considerations. For national collaboration, establishing a strong network of clinical research organizations and institutions along with a Society for Clinical Research Sites in Pakistan is direly needed. Hopefully these measures will bring a positive change in the future landscape of clinical research in Pakistan

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CONFLICT OF INTEREST

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