Details of The research works of Abhijit Chowdhury
In the context of the award

Professor Abhijit Chowdhury is a clinician Scientist who, through his over two decades of impacting research work, has made outstanding contributions in improving the essential understanding of disease mechanisms, contributed in the area of epidemiology as well as disease burden and carried out health system experiments to develop solutions that have potentials for making an impact in his research focus domain. His research has been broad based, particularly in the speciality area of Liver Diseases. Keeping this broad base, Professor Chowdhury focused on Nonalcoholic fatty Liver disease (NAFLD, recently renamed various as MASLD or MAFLD) later on as his research focus. This focus culminated in some publications that had gone a long way in describing the phenotype named Lean NAFLD that had been of spiraling clinical-public health and pathophysiological study interest in relevant discourses in this domain subsequently. It could be a learning for fellow researchers to know how the initial description of the entity named lean NASH , as they did in 2010, was initially received with significant skepticism and cynicism in contemporary peer circles . These initial confusions were overrun as more robust data came in from Dr. Chowdhury's group as well as others who replicated the findings in different populations across the world. Initial description of a phenotype considered as an outlier, meticulous characterization its' pathophysiology and clinical outcomes, generation of hypothesis on mechanism of the disease , creative studies on methods to assess and manage this public health scourge are essential and comprehensive approaches that he pursued to see the issue to be in mainstream global scientific focus today.

Population based analytical epidemiology of liver diseases with relevance in the social context of developing countries had been the research area of interest of Chowdhury all along. All his researches have been driven by this broad intent and philosophy, rather than being "geographical medicine", even before this game changer description on lean NAFLD. This has happened in a sequential manner and he had picked up biological issues of global relevance while planning his research methods as well as strategy. Thus, this community based epidemiology of fatty liver disease came after his previous experiences of epidemiology of Hepatitis viruses in general population of Birbhum that he did beginning in 2003. It is widely known that obese have a propensity to develop NAFLD and Indian population with social affluence are then the obvious subjects for development of NAFLD. However, this subset in our population is not large, has been expanding though very fast. The research question raised by Chowdhury and colleagues in this context was about the magnitude of this problem, if at all, in a population that is a priori not a predisposed one for metabolic disorders. Thus, they picked up a turf that is non classical – rural, rather physically active, lower socioeconomic strata population – to see what is the status of the disease in them and what are the determinants? It came out that fatty liver disease was present even in this population with nearly 9% prevalence, often unassociated with anthropometric obesity. Interestingly , subtle measures of obesity was present in people who had NAFLD even within this population , raising the idea that this could be a "third world phenotype", as they call it in their seminal, thought provoking and highly cited paper published in Hepatology in 2010. It was hypothesized that this was actually adiposity in disguise.

The research paper in the center and its' significance :
***Hepatology.* 2010; 51: 1593 – 1602.**

While this had been generally useful in clinical as well as public health domain for identification and defining metabolic ill health for long periods of time, it soon emerged that anthropometric obesity measures are inadequate as an overarching tool and outlier phenotypes that are not adequately captured by this definition do exist in metabolic diseases that are similar in pathology, if not the same. This was initially apparent in diabetes, the classical metabolic disease. Evidences started accumulating in early 2000 that suggested that diabetes can exist beyond this limited anthropometric framework. As a result, a primary anthropometry based approach is liable to be reductionist way to a biological phenomenon that has wider dimensions. It was also shown in early 2000's, in elegant studies, that Asians have particular propensity to develop metabolic ill health and clinical disease in a disproportionate manner that defies the existing obesity cut offs. There had since been refinement of the definition of anthropometric cut offs in Asian population to extend the outreach of the definition and make it context relevant.

Despite this, hard evidence from large scale population based studies and description of NAFLD was not forthcoming to substantiate these anecdotal and notional murmurs to firm scientific foundation. Working with a rural population cohort in West Bengal, Chowdhury and his colleagues had shown that fatty liver disease and metabolic disorders can exist in people considered sub-threshold for obesity, are physically active instead of being sedentary and are non-affluent in socio economic scales. This observation expanded the territory of fatty liver disease from its hitherto traditional hinterlands of affluent, sedentary, western world diseases to a much larger global population with attendant implications for population health. Their observation of existence insulin resistance (IR) in the lean cohort with NAFLD underscored the significance of IR as the common underlying premises for the metabolic abnormality and NAFLD, even in persons with apparently low adiposity. This implied that the phenotype described in this study was biologically the same or similar to that seen more generally in the western world. In view of the large population size and the ongoing swift socioeconomic as well as lifestyle changes in developing countries, the observations made in this paper entitled "Nonobese population in a developing country has a high prevalence of nonalcoholic fatty liver and significant liver disease (*Hepatology.* 2010; 51: 1593 – 1602)" marked a transition of understanding in NAFLD research and opened up a new window for research in NAFLD in lean individuals.

It is heartening as well as inspiring to note that this paper has been cited almost 250 times by now as a landmark description of the phenotype. The same issue of Hepatology carried an editorial on the paper (May, 2010) that highlighted important contributions of the work. Initially considered as an Asian enigma, NAFLD in lean is now considered as a global phenomenon and as an outlier phenotype of a common health condition, is a subject of intense pathophysiological investigation for development of therapy targets .

Even importantly, the group under his leadership has pursued the domain ever since with progressively refinement of the research questions. Having discovered the entity, the group had been studying different dynamic aspects of evolution, pathophysiology, assessment and therapy plans. Some important subsequent publications that are in tandem include:

A. Studying the dynamics of lean-obese NAFLD matrix (*Hepatology*. 2014: 60A) as determinants of disease evolution.

B. Development of normative values and utility of transient elastography in Indian population (*Hepatology* 2012; 55: 584-593).

C. Genetics and transcriptomics of Non alcoholic fatty liver disease in India , focussing on lean NASH (J Hepatol. 2021; 74(1): 20-30 , Gene. 2021; 775: 145431 , Annals of Hepatology. 2020 :19(5) ;472-481 , J Genet . 2015 ;94:105–113 .)

D. Transcontinental variability of lean NAFLD, joining groups from USA, Brazil, France, India. (Hepatoma Res. 2020; 6: 72)

E. Global Prevalence of Lean NASH: Meta analysis (Hepatology Communications (2020: 4; 953-972).

F. Review and Hypothesis article on Lean NASH: (Hepatology International. 2013; 7 Suppl 2:806-13, Transl Gastroenterol Hepatol. 2020; 5: 16. JHEP Rep. 2019; 1(4): 329-341)

G. Implementation research for development of a Health system solution that could be integrated into the Country's policy for NAFLD (Lancet Reg Health Southeast Asia. 2023 Jan 19;12:100142)

H. Redefining and new nomenclature of Metabolic dysfunction associated steatotic Liver diseases through global multi stakeholders DELPHI consensus – as the sole author from India in the declaration paper (Journal of Hepatology, June24, 2023 online, Hepatology. 2023 online, Annals of Hepatology. Published Online) This change of Nomenclature from NAFLD to MASLD was a protracted process of debates, deliberations – going to have a long lasting impact in understanding of the disease.

Thus, his contribution to the domain had been multidimensional and comprehensive – one that has impact on improving knowledge on one hand and health of people on the other.

There are certain other elements of Professor Chowdhury's work that could be highlighted as attributes of its' significance;

1. Discovery and description of a phenotype of public health significance that has progressively assumed centre stage of discourse. This has happened through astute weaving at the interface of population based clinical epidemiology and Institution-laboratory analysis of pathophysiology. Meticulous planning , generation of data from field epidemiology and analyzing them, extrapolating and expanding this information in Institutional research and development of multi disciplinary, multi institutional research conglomerates for convergence and complementarity of expertise as well as ideas are some of the strengths that has enabled Prof. Chowdhury to emerge as a scientist and more importantly, as a perfect team scientist that helps answer biological questions in a robust way.

2. The grit and consistency with which he has pursued all these against a tide of notions, expanding the domain of significant fatty liver beyond the traditional anthropometrically defined boundaries is noteworthy.

His other notable research works also need mention here as being relevant.

A. He has done fairly significant useful work in generating community-population based epidemiological data in Hepatitis B and C virus infection in India that has informed policy and strengthened evidence for framing of a national control policy based on the population based data base on Hepatitis B and C that is operational currently.
His work on Hepatitis C virus and subsequently Hepatitis B virus (Hepatology, 2003 and Journal of Gastroenterology and Hepatology, 2005) have proved to be important as background data for framing the national viral hepatitis control program in the country. Very recently, Prof. Chowdhury, working in collaboration with a group of scientists of Institute of Virology, University of Maryland did a molecular epidemiological study on Hepatitis B virus in very difficult terrains in Arunachal Pradesh (Hepatology, 2021). An important aim of this study was to evaluate the utility of a data collection and care delivery model in such settings using information technology tools for data capture by trained field technicians. Incidentally, Arunachal Pradesh is the state in India with the highest degree of population prevalence of HBV. This study brought out many features of epidemiology of HBV disease in that area that will help shaping care in this part of the country and can be a model in difficult to access areas elsewhere. Apart from finding the high prevalence as well as genotypes of HBV in that region, this study, through analysis of the HBV genome and correlating that with that of the far eastern countries, had thrown significant light in population migration in India through the North Eastern corridor.

B. As mentioned, an important aspect of research work of Abhijit Chowdhury is his ability and ideations of pursuing clinical research by combining community with hospital based subjects in a defined relevance. Starting from 2008, Prof. Chowdhury has developed a population cohort in the shape of a health and demographic surveillance system (www.shds.in). This Birbhum population cohort (Int J Epidemiol. 2015; 44(1): 98-107) has provided a steady template for many cross sectional and longitudinal studies in metabolic diseases and allied non communicable diseases. Significantly, the impetus for development of this cohort (2008) and pursuing this was triggered by the work Prof. Chowdhury did in geographically the same area as in his earlier studies in Epidemiology of Liver Diseases including the lean NAFLD study as well as studies on epidemiology of Hepatitis B and Hepatitis C viruses (mentioned below). This cohort has served as a template for many community based downstream studies that has shown that Non-communicable diseases are the primary cause of death in rural population, physical inactivity is widespread, determinants of metabolic syndrome and diabetes in rural population, correlates of overweight and obesity in rural population and many other aspects of metabolic ill health. These field-based studies had provided fair amount of epidemiological and policy pertinent information that were be useful in implementing the NAFLD national policy that India has undertaken as the first country in the world.

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3. As a clinician with an inquisitive and analytical mindset, Prof. Chowdhury has pursued diverse areas of liver disease with NAFLD in lean as the bull's eye in his research spanning more than two decades. He was also engaged in more basic as well as applied research in other clinical and public health domains. This diversity of interest despite maintaining focus is an outcome of his perennially questioning scientific mind and ability to dissect research issues with precision and his publications are testimony to that. In his passionate pursuit of public health as a discourse, he has innovated interventions in rural health care delivery and the impact of that intervention was published in Science (The impact of training informal health care providers in India: A randomized controlled trial. *Science. 2016; 354 (6308). pii: aaf7384.)*. Very encouragingly, this intervention was accepted as a policy by the State Government of West Bengal in 2018 and is being implemented as a rural health care intervention of priority.

   The note as outlined above is a sketch of all that Professor Chowdhury has done so far and keeps on doing as a physician-scientist and an organizer. His research has contributed to widespread consideration of need for a reappraisal of a biased BMI-driven approach to NAFLD. His investigative work has changed the current landscape of knowledge and brought a new paradigm in our understanding of liver diseases and spawned an entire field that is now realizing that lean subjects should not be overlooked in clinical practice and can develop the full spectrum of metabolic comorbidities and liver damage that occurs in non-lean patients. His studies have fuelled a tremendous surge of interest in NAFLD by the key health care stakeholders: patients, providers, payors, and policymakers and provides the framework for formulating strategies for the screening, management, and treatment of NAFLD.