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Please tell us what you are working on and what impact do you hope it will have?

The growing burden of Type 2 Diabetes Mellitus in India is of concern. The primary targets of insulin action to maintain glucose homeostasis are the skeletal muscle, liver, and adipose tissue. Among these, skeletal muscle is considered to be the largest insulin-sensitive organ. Despite normal body mass index, many Indians may be at risk of becoming insulin resistant, raising the possibility, that insulin resistance is related more to regional rather than general adiposity. Fat storage in non-adipose tissue could exist independent of generalized adiposity making it difficult to establish true associations between insulin resistance and body mass index. The present standard recommendations to either prevent or treat Type 2 Diabetes, are modifications in lifestyle habits. With a pre-existing low muscle mass, it will be very important to evaluate the impact of caloric restriction, protein supplementation and resistance exercise in regulating and maintaining insulin sensitivity in Indian population. We are working towards understanding the role of skeletal muscle in the aetiology of Type 2 Diabetes in the Indian population and to evaluate the efficacy of interventions designed to target improvements in muscle mass, function and metabolic potential. A better understanding of the cause(s) of the predisposition of Indians to become Type 2 Diabetes will be very useful in evolving healthcare policy.

Can you share some interesting findings from your research on "thin-fat Indians"?

Asian Indians are thought to have a greater propensity for a phenotype that is characterized by an excessive accumulation of fat for a normal body mass index (BMI) (kg/m^2), which has been termed 'metabolically obese', or simply 'thin-fat'. They have also been demonstrated to be at a greater risk of becoming profoundly insulin resistant, even with a normal BMI, suggesting that their insulin resistance is related more to regional (muscle) rather than general adiposity. There is little information about intramyocellular fat (IMF) among Indians with prediabetes. As part of the cross-sectional component of my studies, quantitative histological examinations of biopsied quadriceps muscle cells from individuals with prediabetes and their age-matched controls were performed. These groups of individuals were comparable in terms of their BMI, muscle to fat ratio and beta cell function. Oil red O staining performed on biopsied tissue sections to identify their lipid content demonstrated a higher lipid accumulation in prediabetes group, such that the proportion of total area occupied by IMF was thrice than seen in controls. In comparison with Western populations with Type 2 diabetes, the skeletal muscle IMF content of Indians with prediabetes was 3 times higher. The current analysis provides proof of the existence of ectopic fat (IMF) among Indians with prediabetes. Further my fellowship will be able to evaluate the mechanisms that lead to the deposition of IMF and how reversible this phenomenon could be with lifestyle intervention programs such as exercise and diet.

Is there a research area other than yours that interests you deeply?

Apart from working in the field of chronic diseases especially Type 2 Diabetes, I have always been intrigued with the process of ageing. There is always a difference in biological ageing *versus* chronological ageing. To lead a healthy and longer life it is important to focus on biological ageing. Evaluating factors modulating ageing and improving quality of life of an elderly through interventions interests me. In addition, being associated with skeletal muscle research of late, I have developed interest in understanding mechanisms underlying biomechanics especially in an athlete.

How has Wellcome Trust/DBT India Alliance funding helped you and your research?

The structure of fellowship program, flexibility in funding and platform provided for the fellows to setup and execute ideas is a blessing. The Wellcome Trust/DBT India Alliance fellowship gave me confidence and liberty to achieve things which otherwise would have been difficult. The Intermediate Fellowship gave me a platform to setup independent lab, explore, collaborate and translate research. The lifestyle modification program customized as part of the fellowship is now being accepted by the front end clinicians after seeing the benefits to the patients. The skeletal muscle function lab has gained momentum by itself, with clinicians wanting to evaluate skeletal muscle functional assessment for various clinical conditions. This fellowship allowed me to achieve my dreams of having an independent setup, test ideas and adapt it to see transformations.



Above: Sucharita's muscle function lab



Below: Study participant undergoing gym training as part of the lifestyle modification program

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INDIA ALLIANCE FELLOW IN SPOTLIGHT

Dr. Sucharita Sambashivaiah



How was your transition from being a clinician to a public health researcher? Any specific challenges you faced as a woman researcher?

I have been heading a Clinical Service Unit since couple of years now. The fact that I have been able to provide diagnosis and help in the treatment aspect has always sustained me to run the unit, in spite of challenges which accompanies it. The field of public health research has given me platform to help people at a larger scale. The transition for me has been really enjoyable and would recommend clinicians go through the same. The Wellcome Trust/DBT Indian Alliance fellowship offers clinicians to work closely with human disease-related questions. I believe if more and more clinicians could be part of such programs, future of Indian clinical research will be bright. Being a woman researcher I have not specifically faced any challenges. There are challenges which each and every researcher goes through, it is the way one looks at it and overcomes with positive attitude that matters.

Any advise (from your own personal experience) for clinicians hoping to make the same transition?

As a teacher to medical students, I feel it is high time we start sensitizing our medical graduates about the process and benefits of doing medical research. It should start early to have a greater impact later. In addition, the advantage of being a clinician one will be in a first-hand position to ask clinically-relevant research questions. Based on my experience one could translate some component of the research questions effectively. I would highly recommend young clinicians to utilize opportunity provided by fellowships offered by the India Alliance.

What keeps you going everyday?

Being able to face challenges every day and overcome it keeps me going. The hope and belief that the clinical research will soon help patients keeps me motivated. The ability to fill hope and aspiration among young researchers and clinicians makes me work harder. Last but not least is the highly inspiring work environment in my

department motivates me to reach newer heights.



Sucharita and her team regularly conducts medical camps to increase awareness of Pre-diabetes as part of the public engagement aspect of the fellowship