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Highlights of the Research Retreat on Diabetes in Pakistan

Dear Readers,

We are excited to share the highlights of the recent Research Retreat event, organised by R&D Department at TDC. The aim of this retreat was to invigorate the Research Committee, fostering an environment conducive to brainstorming and the generation of innovative research ideas. The dynamic leadership of **Dr. Imran Mirza and Dr. Asrar Ahmad** played a pivotal role in steering the event towards its objectives.



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The retreat unfolded as a vibrant and insightful session, marked by engaging discussions and knowledge exchange. Participants actively contributed to the exploration of three crucial dimensions of diabetes research: **Epidemiology and Risk Factors, Challenges in Management and Treatment, and Innovations and Future Research Directions.**

The retreat flourished as a collaborative platform where diverse perspectives converged. Looking ahead, the Research Committee will further refine and develop the identified research ideas.

TDC Speaker Series: Bridging Knowledge Gaps for Better Patient Care

We are thrilled to share exciting updates as we continue to expand our commitment to education and knowledge-sharing within the medical community. Our Education Committee has been diligently working to organize a weekly Speaker Series, featuring renowned international experts who deliver insightful lectures on various aspects of diabetes care.

In our recent sessions, we had the privilege of hosting distinguished speakers who shared their expertise on critical topics that directly impact the field of diabetes management. Let's take a closer look at the enlightening sessions we've had:

1. Dr. Aly Bernard Khalil

Senior Consultant, Head of Endocrinology, Al Reem Hospital, Abu Dhabi, UAE

Topic: Pregnancy and Hypothyroidism

2. Dr. Muhammad Badar uz Zaman

Division Chief & Head of Transplant, Sheikh Khalifa Medical City, Abu Dhabi, UAE

Topic: Options for Patients with Diabetes Related Renal Failure

3. Dr. Moutaz Osman

Senior Consultant Endocrinologist, King Fahad Military Medical Complex, Dhahran, Saudi Arabia

Topic: Role of once weekly GLP1RA in outcomes of T2D patients

4. Dr. Sharjeel Sarfraz

Consultant Urologist, Institute of Urology & Transplantation, Rawalpindi, Pakistan

Topic: Diabetes & Sexual Health of Men

These engaging and informative lectures provide valuable insights into the latest developments in diabetes care and its intersection with various medical specialties.

At TDC we are committed to fostering a culture of continuous learning and collaboration. The Speaker Series is just one of the many initiatives we undertake to stay at the forefront of diabetes care and provide our patients with the best possible outcomes.

We encourage all our staff to take advantage of this valuable resource and stay tuned for more enriching sessions in the coming weeks.

Featured Research

Gut Microbiota Linked to Statin-Associated New-Onset Type 2 Diabetes

The human gut microbiota has been linked to an increased risk of statin-associated new-onset type 2 diabetes, as revealed by findings published in *Arteriosclerosis, Thrombosis, and Vascular Biology*. While statin use has previously been associated with an elevated risk of type 2 diabetes, recent research has indicated that changes in the microbiota due to statin use might contribute to this risk.

To investigate the potential role of microbiota in the risk of type 2 diabetes among statin users, researchers conducted a retrospective analysis using data from the Finnish cohort FINRISK study. Fecal samples from the 2002 cohort and register-based follow-up data were used to examine the relationship between gut microbiota and diabetes risk over a 17-year follow-up.

The study included 393 statin users and 5,362 non-users. Statin users were found to have a higher average age, a higher proportion of men, higher systolic blood pressure, increased use of antihypertensive, metformin, and psychotropic drugs, as well as lower cholesterol levels compared to non-users. Statin use was associated with changes in beta-diversity, with 26 species showing significant associations.

The incidence of type 2 diabetes among statin users and non-users was 16.3% and 5.2%, respectively. Beta-diversity was linked to a higher risk of incident type 2 diabetes. The researchers identified an association between type 2 diabetes risk and a total of 24 species, with *Bacteroides vulgatus* associated

with the highest risk and *Butyrivibrio crossotus* associated with the lowest risk.

In an analysis considering incident statin use during follow-up, statin-associated new-onset type 2 diabetes risk was associated with specific species.

The study suggests novel associations between statin use and the gut microbiota, providing insights into microbiota features that may influence the risk of statin-associated new-onset type 2 diabetes. The findings offer potential tools for studying and understanding the pathogenesis of the disease, ultimately contributing to the definition of a health-promoting gut microbiota profile in the future. Study limitations include the absence of longitudinal microbiome data, unknown medication adherence, and potential variations in effects among different statins.

Teplizumab-MZWV: A Breakthrough in Delaying the Onset of Type 1 Diabetes

Teplizumab-MZWV, a humanized IgG1 kappa CD3-directed monoclonal antibody, has gained FDA approval as the first drug capable of delaying the onset of type 1 diabetes (T1D). T1D, an autoimmune condition resulting from T cell-mediated destruction of pancreatic β cells, leads to insulin deficiency, compromised glycemic control, and dependence on exogenous insulin. Originally employed to prevent graft-versus-host disease in organ transplantation, anti-CD3 therapy has recently been investigated for its potential to extend the onset of T1D in high-risk patients. Teplizumab targets T cells through antibodies against the T cell receptor (TCR) component CD3, with its mechanism of action suggesting partial agonistic signaling and deactivation of autoreactive T lymphocytes in pancreatic beta cells. Crucially, teplizumab was designed as an Fc-non-binding antibody to mitigate the risk of severe adverse effects related to cytokine release syndrome (CRS). This syndrome can occur when Fc-receptors bind to the "tail-end" of anti-CD3 antibodies in an antigen-non-specific manner.

A pivotal phase 3 randomized, placebo-controlled trial evaluated β -cell preservation, clinical endpoints, and safety in children and adolescents undergoing two 12-day courses of teplizumab or placebo. The primary endpoint, a change in β -cell function measured by stimulated C-peptide levels at week 78, revealed a significant advantage for teplizumab-treated patients. These individuals exhibited higher stimulated C-peptide levels compared to the placebo group, with

94.9% maintaining a clinically meaningful peak C-peptide level of 0.2 pmol per milliliter or greater, as opposed to 79.2% in the placebo cohort.

While the groups did not differ significantly in key secondary endpoints, the safety profile indicated manageable adverse events, including headache, gastrointestinal symptoms, rash, lymphopenia, and mild cytokine release syndrome, primarily associated with teplizumab or placebo administration.

The FDA's approval of teplizumab marks a significant milestone in diabetes care, offering new hope for delaying the onset of type 1 diabetes in high-risk individuals. The positive outcomes from the phase 3 trial underscore the potential of teplizumab as a transformative therapy in the realm of autoimmune conditions.

Telemedicine in Diabetes Care Associated With Worse Outcomes

A recent retrospective cohort study conducted by OPLINE has indicated that adult patients with type 2 diabetes and complex care needs may experience worse glycemic outcomes when receiving endocrinology treatment exclusively through telemedicine. In contrast to some earlier studies suggesting comparable glycemic outcomes between telemedicine and in-person care for type 2 diabetes management, this research focused specifically on endocrinology settings and clinical factors influencing treatment complexity.

The study encompassed 3,778 adults with type 2 diabetes within a large integrated US health system, who received care through telemedicine-only, in-person, or a combination of both modalities between May and October 2020. Patients were followed up through May 2022, evaluating estimated A1c changes after 12 months within each treatment cohort and examining associated factors.

The findings revealed that patients receiving telemedicine-only care showed no significant changes or improvements in adjusted A1c over the 12-month evaluation period. In contrast, those receiving in-person care demonstrated an improvement of 0.37%, while patients receiving mixed care exhibited an improvement of 0.22%. The patterns remained consistent among patients with a baseline A1c of 8% or higher.

Patients prescribed multiple daily injections versus no insulin experienced a 0.25% higher estimated change in A1c with telemedicine compared to in-person care. No significant associations were observed between changes in A1c and comorbidities.

The authors of the study attributed the differences to

the potential limitations of telemedicine in delivering essential components of diabetes care, such as self-management education support, during virtual visits. They emphasized the need for the implementation of strategies, including team-based virtual care and technological tools for blood glucose data sharing, to bridge the gap and ensure high-quality diabetes care through telemedicine.

The study's implications suggest that patients relying solely on telemedicine for endocrinology care may require additional support to achieve glycemic goals. As telemedicine continues to be a vital mode of care, the authors emphasized the necessity for structured approaches to ensure routine delivery of high-quality team-based diabetes care, especially for patients with complex diabetes. The translation of successful strategies from clinical trials into routine telemedicine care was highlighted as crucial for improving clinical outcomes in this patient population.

Rheumatoid Arthritis Drug Could Put Brakes on Type 1 Diabetes

A potential breakthrough in the management of type 1 diabetes has emerged, with Australian researchers investigating the repurposing of the rheumatoid arthritis drug, baricitinib (Olumiant). The study, led by Dr. Thomas Kay of St Vincent's Institute of Medical Research in Melbourne, focused on the drug's ability to preserve the natural insulin production capacity in newly diagnosed type 1 diabetes patients.

Type 1 diabetes, constituting approximately 5% of all diabetes cases, results from the immune system erroneously attacking pancreatic beta cells responsible for insulin production. Traditionally, individuals with type 1 diabetes rely on injected insulin for survival. Dr. Kay's trial demonstrated that early administration of baricitinib post-diagnosis maintained insulin production in participants, resulting in significantly reduced reliance on insulin therapy.

The study, the first human trial centered on baricitinib for type 1 diabetes, involved 91 newly diagnosed individuals aged 10 to 30, tracked over a year. Participants were divided into two groups: one receiving baricitinib and the other a placebo. The trial assessed blood sugar levels, insulin production, and the drug's impact on disease progression.

Baricitinib operates by blocking an enzyme linked to immune system regulation and inflammation, curbing the immune response responsible for the destruction of pancreatic beta cells. Administered early in the disease progression, the drug proved effective in preserving

insulin-producing cells. While none of the participants could fully wean themselves off insulin therapy, those given baricitinib required significantly less insulin for treatment. Continuous glucose monitoring demonstrated improved blood sugar control, indicating the drug's potential in managing type 1 diabetes.

The study, funded by JDRF (formerly the Juvenile Diabetes Research Foundation), holds promise for a paradigm shift in type 1 diabetes management. Co-author Helen Thomas expressed optimism about the treatment becoming clinically available, marking a substantial advancement in controlling and treating type 1 diabetes. Further research may be necessary to fully understand the drug's potential and refine its application in clinical settings.

Interesting Case Report

Chronic Venous Ulcer

A 60-year-old male patient, known to be diabetic for approximately 15 years, presented at the TDC Outpatient Department (OPD) with a one-year history of a non-healing wound on his left leg. Additionally, the patient had recently been diagnosed with hypothyroidism and Parkinsonism. Despite consulting various doctors and undergoing extensive antibiotic treatments, both systemic and local, the wound showed no signs of healing as he was being treated on the lines of diabetic foot ulcer. The patient also exhibited skin changes around the lateral malleolus and experienced an increase in swelling upon movement, leading to reluctance in performing routine daily activities.



First Visit



Most Recent Visit

The patient sought consultation with Dr. Faizan at TDC. A preliminary diagnosis of chronic venous insufficiency with a non-healing ulcer was made. An ankle-brachial index (ABI) was conducted, yielding normal results. Subsequent ultrasound examination revealed varicose veins with below-knee thrombophlebitis but no junctional incompetence, indicating perforator reflux. Arterial

scanning, however, showed normal results. Based on these findings, foam sclerotherapy for perforator reflux with compression bandages was recommended, although the patient declined any internal intervention and opted for compression bandages alone.

Compression bandages were applied from the foot to the knee joint, and the wound was maintained in a clean condition using tropical antibiotics. No systemic antibiotics were administered, in accordance with the culture report. Dressings were changed every 48 hours, and the patient was instructed to mobilize normally as needed.

During follow-up visits, gradual improvement was observed in the wound, with the patient reporting reduced pain and swelling. After six weeks of consistent monitoring and follow-up, the wound had nearly epithelized, indicating complete healing. The patient will now transition to grade 2 compression stockings for a duration of six months to support continued recovery and prevent recurrence. This case highlights the successful management of a non-healing Chronic Venous ulcer by addressing underlying venous insufficiency through a combination of compression therapy and patient compliance with recommended interventions.

Educational Resources

ADA Issues New Screening, Obesity Management Recommendations

The American Diabetes Association (ADA) has issued new recommendations in its Standards of Care for 2024, encompassing a range of updates aimed at enhancing the management of individuals with diabetes and those at risk. Developed through a comprehensive scientific literature review by the ADA's Professional Practice Committee, the document covers key aspects of diabetes care and has received endorsements from organizations such as the American College of Cardiology, the American Society of Bone and Mineral Research, and the Obesity Society.

One significant update involves the introduction of screening recommendations for heart failure, emphasizing the measurement of natriuretic peptide levels in adults with diabetes to detect asymptomatic heart failure. Another notable addition is the recommendation for screening peripheral arterial disease (PAD) using ankle-brachial index testing in asymptomatic individuals aged 50 years and older with diabetes, particularly those with microvascular disease,

foot complications, or end-organ damage.

The ADA's 2024 Standards of Care also feature new screening protocols for type 1 diabetes, emphasizing islet autoantibody tests and diagnostic criteria for preclinical stages.

Obesity management, regular evaluation and treatment of bone health, assessment of disability with guidance for referral, and alignment of liver disease screening and management are also included. Clinicians are encouraged to download the Standards of Care app on their smartphones for quick reference, providing a valuable resource for addressing questions that may arise during patient care.

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Feedback

We are excited to hear from you. Please send us your feedback at rc@tdc.com.pk

"Health is not valued till sickness comes."

Thomas Fuller