## Medical News

### Factor Xa Inhibitors Tied to Interstitial Lung Disease in Atrial Fibrillation

Medscape

November 23, 2022

In patients with non-valvular atrial fibrillation (NVAF), treatment with factor Xa (FXa) inhibitors was associated with a greater risk of interstitial lung disease (ILD) than other oral anticoagulants (OACs), a medical records analysis shows.

Emerging concerns from case reports and pharmacovigilance analyses of a possible risk of ILD associated with the use of FXa inhibitors prompted the analysis, said Gregory Lip, MD, of the University of Liverpool and Liverpool Heart & Chest Hospital, UK.

"This is an observational study which describes associations, not causality," Lip told theheart.org | Medscape Cardiology. "Thus, this requires further studies in different populations and additional prospective work or clinical trials."

The researchers plan to initially look to see if the findings can be replicated in studies of other large cohorts, including non-Asian studies, he said. Meanwhile, "vigilance in monitoring for any potential adverse lung outcomes associated with the use of these drugs is recommended as part of the holistic approach to AF care and management," he said.

And they are not advocating that patients change back to warfarin, the authors note. The absolute difference in rates of ILD between the FXa inhibitors and warfarin was small (0.12 per 100 patient-years) and much lower than the absolute reduction in the incidence of thromboembolism (0.78 per 100 patient-years) and major bleeding (0.78 per 100 patient-years) between the FXa inhibitor and warfarin groups, they point out.

The cohort study of more than 100,000 patients in Taiwan was published online November 22 in JAMA Network Open.

The analysis of data from the Taiwan National Health Insurance Research Database included 106,044 patients with NVAF (mean age, 73.4 years; 56.6% men) without pre-existing lung disease who were treated with OACs from 2012 to 2017. The authors used propensity score stabilized weighting (PSSW) to balance covariates across the medication groups (FXa inhibitors, dabigatran, and warfarin, with warfarin as the reference).

Patients were followed from the drug index date until the onset of ILD, death, or study end (December 31, 2019). Among the 60.9% of patients treated with FXa inhibitors, 24% received apixaban; 19%, edoxaban; and 57%, rivaroxaban. In addition, 21.2% received dabigatran and 17.9% received warfarin at baseline.

After PSSW, FXa inhibitors were associated with a higher risk of incident ILD (0.29 vs 0.17 per 100 patient-years; hazard ratio [HR], 1.54) and dabigatran was associated with a nonsignificant risk difference.

Furthermore, patients who were diagnosed with ILD during follow-up and treated with FXa inhibitors had a higher risk of ILD requiring consequent antifibrotic agents than those treated with warfarin (odds ratio, 3.01).

The higher risk of incident ILD for FXa inhibitors versus warfarin was consistent within several high-risk subgroups, such as those taking amiodarone (0.38 vs 0.26 per 100 patient-years; HR, 1.41). The risk also was higher with dabigatran (0.31 vs 0.18 per 100 patient-years; HR, 1.62), and warfarin (0.28 vs 0.13 per 100 patient-years; HR, 1.97). The lowest risk of ILD was in patients treated with warfarin without amiodarone.

Study limitations included the reliance on claims instead of clinical data on ILD; an older patient population with AF who may already have had a higher overall risk of incident ILD; lack of laboratory data on patient liver and kidney function, which may have affected treatment decisions; and enrollment of only Asian patients.

### New Agent: 'First Step' Toward Delaying Progression of Type 1 Diabetes

Medscape

November 22,2022

The US Food and Drug Administration (FDA) has just approved teplizumab (Tzield) for the delay of clinical type 1 diabetes in people age 8 years or older who have stage 2 type 1 diabetes.

Stage 1 type 1 diabetes means that someone has beta-cell autoimmunity and normal glucose levels. Beta-cell autoimmunity means that someone has two or more islet autoantibodies present; that means anti-insulin antibodies, GAD65, IA-2, and/or the zinc transporter autoantibodies. All of these are commercially available, so you can measure them in your patients. If they have two or more that are positive and normal glucose levels, they are considered stage 1. These people are presymp-

tomatic. They don't know they are at risk for type 1 diabetes unless you measure their autoantibodies.

Stage 2 type 1 diabetes is really prediabetes in someone who's going to get type 1 diabetes. They have evidence of beta-cell autoimmunity, but now they have dysglycemia and they're presymptomatic. They basically have an impaired fasting glucose level ≥ 100. They have abnormal glucose levels on a glucose tolerance test. Unlike with pre–type 2 diabetes, there are glucose levels at intermediate time points of 30, 60, and 90 minutes that can also make the diagnosis and/or they have an A1c level ≥ 5.7%. These are people who have the autoantibodies, and you see that they have prediabetes.

One of the problems is that we use the same criteria, by and large, that have been developed to look at prediabetes in people with type 2 diabetes. There's ongoing research looking at the optimal values for predicting the rate of progression to the onset of symptomatic type 1 diabetes in these people. Symptomatic type 1 diabetes is considered stage 3.

People with stage 3 type 1 diabetes now fit the glycemic definition of diabetes, and they have the presence of two or more autoantibodies. At stage 2, there is a very high risk that someone is going to go on to develop stage 3 type 1 diabetes. There is a 60% risk that someone will develop overt type 1 diabetes in 2 years and a 75% risk that it will develop over the next 4-5 years. We really want to try to do something with those patients at stage 2 so that they don't go on to develop stage 3 or clinically significant type 1 diabetes.

Teplizumab works to slow the progression from stage 2 type 1 diabetes to stage 3 or clinically significant type 1 diabetes. It is the first approved disease-modifying agent for type 1 diabetes. It demonstrates a median 2-year delay in the progression from stage 2 to stage 3 type 1 diabetes. It is an anti-CD3 monoclonal receptor-nonbinding antibody.

The study used for approval of teplizumab included 76 participants with stage 2 type 1 diabetes; 44 patients were randomized to the teplizumab group and 32 to the placebo group. The drug is given as a daily infusion for 14 consecutive days. Patients were then followed for a median of 51 months.

The time to diagnosis of type 1 diabetes was 48.4 months in the teplizumab group and 24.4 months in the placebo group. The disease was diagnosed in 43% of the participants who received teplizumab vs 72% who received placebo. Looked at another way, the annualized rates of the diagnosis of stage 3 or clinical type 1 diabetes were about 15% per year in the teplizumab group and approximately 36% per year in the placebo group. This represents a statistically significant delay in the development of stage 3 type 1 diabetes.There were no unexpected side effects, but they did see adverse events of rash, headache, and transient lymphopenia.

"I know we would all love a cure for type 1 diabetes, or at least the ability to completely prevent progression to type 1 diabetes, but teplizumab really opens the door. It's the start for our doing something to help prevent or at least slow the progression to developing stage 3 type 1 diabetes. I think first steps are first steps.

One of the really important factors here lies in how much we will be screening people for pre–type 1 diabetes. I want to see how this really impacts people, particularly children, because I think that for a young child, to develop type 1 diabetes is really overwhelming and requires a great deal of change in their life. If that can be slowed — the progression to needing insulin, needing to poke their fingers, or using an insulin pump — I think all that may be very impactful.

This is the first time ever we've been able to slow the progression of type 1 diabetes through the stages" said by Anne L. Peters, MD who is a professor of medicine at the University of Southern California (USC) Keck School of Medicine and director of the USC clinical diabetes programs.

**ACR, EULAR Roll Out Updated Antiphospholipid Syndrome Criteria**

Medscape

November 22,2022

A draft update of criteria for classifying antiphospholipid syndrome (APS) incorporates a much broader spectrum of disease signs and symptoms, such as kidney disease and more variables for pregnancy, and meets a higher level of specificity than the existing Sapporo criteria, although at the expense of lower sensitivity.

Three members of the core planning group that wrote the update, jointly commissioned by the American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR), reviewed the proposed criteria at the annual meeting of the ACR.

If ACR and EULAR adopt the new criteria, it would be an update to the Sapporo classification criteria for APS, which was last updated in 2006. The pending criteria consist of the following eight domains encompassing clinical findings and laboratory test results:

- Macrovascular — venous thromboembolism (VTE) with and without high VTE risk profile.
- Macrovascular — arterial thrombosis with and without a high cardiovascular disease risk profile.
- Microvascular — additional categories for kidney disease, pulmonary embolism, and other conditions for both suspected and established APS.
- Obstetric — expanded definitions to account for

the absence or presence of preeclampsia or premature birth with or without fetal death.

- Cardiac valve — accounts for thickening and vegetation.
- Hematologic — includes thrombocytopenia (defined as the lowest platelet count, 20-130 × 109/L).
- Antiphospholipid (aPL) test — coagulation-based functional assay, assigning greater weight to persistent over one-time positive test results.
- aPL test by solid-phase assay — includes anticardiolipin enzyme-linked immunosorbent assay (aCL ELISA), and aCL/anti-beta 2 glycoprotein-I (aCL/anti-beta 2 GPI) tests, with greater weight assigned for moderate-to-high positive results depending on isotype, whether immunoglobulin G or M.

### Changes from Sapporo Criteria

The existing Sapporo criteria include two clinical categories, vascular thrombosis and pregnancy morbidity; and three laboratory categories, positive lupus anticoagulant, medium or high antibody titers, and high aCL/anti-beta 2 GPI measured by ELISA. All of these are included in the draft criteria under two domains.

"These novel clinical features will help us better stratify patients according to the risk factor profile," Stéphane Zuily, MD, PhD, a vascular specialist and European co-principal investigator of the planning group, said in explaining the proposed updated domains.

**Your Patients Are Rotting Their Teeth With Vaping**

Medscape

November 22,2022

Primary care physicians, and especially pediatricians, should consider telling their patients about the long-term oral health problems associated with vaping.

A new study found that patients who use vapes were at a higher risk of developing tooth decay and periodontal disease.

Vapes were introduced to the US market in 2006 as an alternative to conventional cigarettes and have become widely popular among youth. According to a 2022 survey from the US Centers for Disease Control and Prevention, 2.55 million middle and high school students in this country reported using the devices in the previous 30 days.

The new study, published in the Journal of the American Dental Association, expands on an initial case series published in 2020 of patients who reported use of vapes and who had severe dental decay. Karina Irusa, BDS, assistant professor of comprehensive care at Tufts University, Boston, Massachusetts, and lead author of the case series, wanted to investigate whether her initial findings would apply to a large population of vape users.

For the new study, Irusa and colleagues collected data on 13,216 patients aged 16-40 who attended Tufts dental clinics between 2019 and 2021. All patients had received a diagnosis of tooth decay, had a tooth decay risk assessment on record, and had answered "yes" or "no" to use of vapes in a health history questionnaire.

Patients had records on file of varying types of dental lesions, cavities filled within the previous 3 years, heavy plaque on teeth, inadequate brushing and flushing, and a self-report of recreational drug use and frequent snacking. If patients had these factors on their file, they were at high-risk of developing decay that leads to cavities.

The study found that 79% of patients who responded "yes" to being a current user of vapes were at high risk for dental decay, compared with 60% of those who did not report using the devices. Materials in the vaping liquids further cause an inflammatory response that disrupts an individual's internal microbiome, according to numerous studies.

"All the ingredients of vaping are surely a recipe for overgrowth of cavities causing bacteria," said Jennifer Genuardi, MD, an internist and pediatrician at federally qualified community health center Urban Health Plan, in New York City, who was not involved in the study. Irusa said information on patient's vaping habits should be included in routine dental and medical history questionnaires as part of their overall electronic health record.

"Decay in its severe form not only affects one's ability to eat but affects facial aesthetics and self-esteem as well," Irusa said. Genuardi called the findings unsurprising.

"We are learning daily more and more about the dangers of vaping," Genuardi said. "There's a focus of today's research on the effect of actions on our microbiome and the subsequent effects on our health."

Genuardi also said many of her teenage patients do not enjoy dental visits or having cavities filled, which could serve as a useful deterrent to vaping for a demographic that has been targeted with marketing from vape manufacturers.

"Cavity formation and the experience of having cavities filled is an experience teens can identify with, so this to me seems like perhaps an even more effective angle to try to curb this unhealthy behavior of vaping," Genuardi said.

**Psim News Corner:**

The 1st ever PSIM International Medical Conference,

November 2022, Dubai UAE

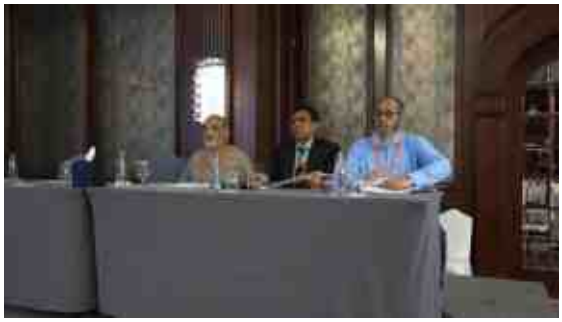
PSIM had its 1st ever international appearance with a Medical Conference in Dubai from 4$^{th}$ to 6$^{th}$ November

with a theme of "Updates on Internal Medicine". The conference brought together experienced physicians and specialists from all across the world to discuss the most complex global challenges in the field of medicine. The conference provided the opportunity for healthcare practitioners, researchers and professionals to share their experiences, challenges and solutions to deliver better healthcare to all. It brought forth a platform for multi-disciplinary discussions from different institutions. There were different sessions covering all the nooks and corners of medicine with recent updates. Without doubt, all the sessions witnessed exemplary discussions about both common as well as rare medical conditions with active involvement by the participants.

Pakistan Society of Internal Medicine (PSIM)'s core leadership visited "The Health Bank Global, Dubai's headquarter on 5th November 2022. The delegation of PSIM was led by it's President Prof Dr Javed Akram, along with SVP, Prof Aftab Mohsin, Gen Sec Associate Prof Dr Somia Iqtadar on invitation of Dr Suhail Chughtai, the Chief Technology Officer of the Multi-national Telehealth Firm, "The Health Bank Global", based in Dubai. The delegation was given briefings on Remote Disease Management on Clinical Telemedicine systems.

A delegation of Pakistan Society of Internal Medicine also visited PMC (Pakistan Medical Centre) on invitation of Pakistan Association Dubai (PAD). Dr Faisal Ikram President PAD and Dr Zafar Iqbal Gondal Joint Secretary PAD conducted a guided tour of the health facility.

This was followed by a detailed discussion on areas of mutual collaboration on health projects and academic activities between PSIM and PAD. An MOU was also signed by the two organizations for collaboration related to research, academic activities and health initiatives.




MÖVENPICK


4th to 6th November 2022
Dubai, UAE
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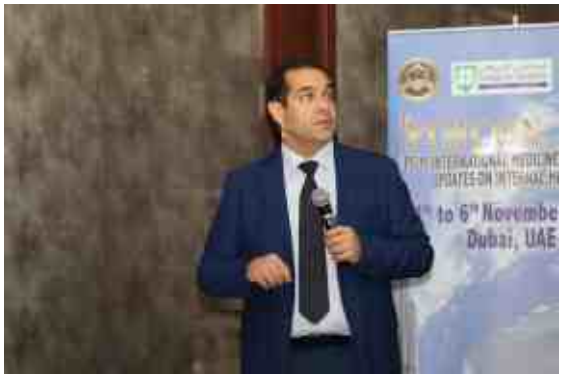
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**World Diabetes Day Seminar: 19 Nov 2022**

World Diabetes Day Awareness activity was organized by the Pakistan Society of Internal Medicine in collaboration with Express Media forum at Pearl Continental Hotel Lahore on Saturday, 19th November 2022. Prof. Dr. M. Zaman Shaikh, Prof Javed Akram, Dr.Somia Iqtadar, Prof Gulshad, Prof Tariq Waseem, Prof Sajid Abaidullah, d Dr Imtiaz Hasan and Dr Shehla Javed Akram created awareness regarding different issues related to diabetes. This was an awareness session on diabetes for the general public by PSIM for a better understanding of diabetes and related problems.

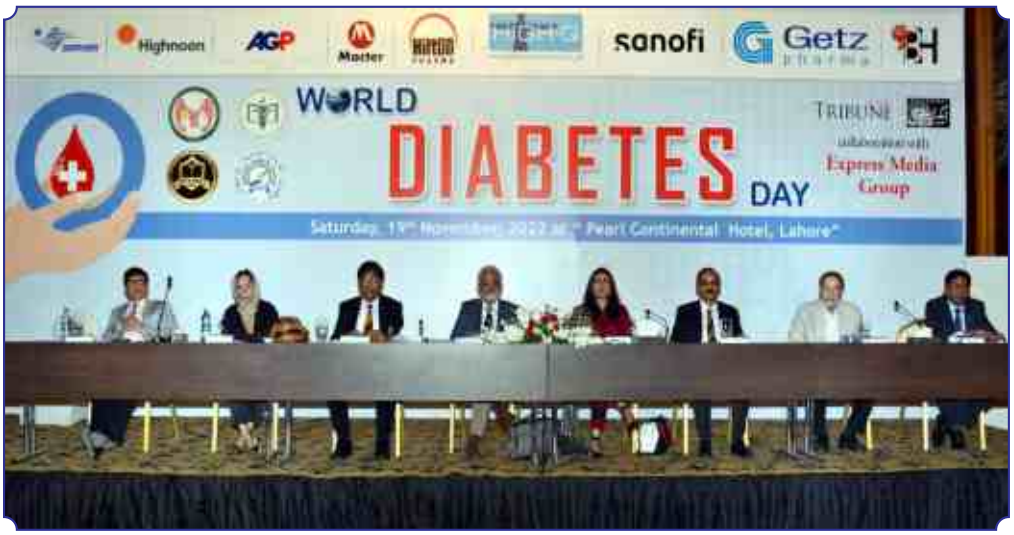
PSIM Secretary General Dr. Somia Iqtadar also announced the launch of PNDP (PSIM Network for Diabetes Prevention) a volunteer force to work on awareness and action to Prevent Diabetes in the country which will be led by President PSIM Prof Javed Akram and Chair for National Diabetes Chapter PSIM Prof Zaman Sheikh.

**Presidential Award of Excellence:**

This November our star-studded PSIM achieved some new heights of excellence as our top-notch faculty got appreciated for dedication and commitment to work and for selfless services for the humanity. The honorable President of the Islamic Republic of Pakistan Dr. Arif Alvi awarded Excellence Awards to ten distinguished physicians of the country for their contribution to Diabetes care in Pakistan on 15th November 2022 at President House Islamabad to commemorate World Diabetes Day.

President PSIM Prof Javed Akram, Secretary General PSIM Dr.Somia Iqtadar, and Prof Rauf Niazi Federal Chapter Head PSIM are the proud recipients of this award.

Whole PSIM faculty is proud of them for achieving this award and congratulates them with a wish to see them outshine and prosper day by day.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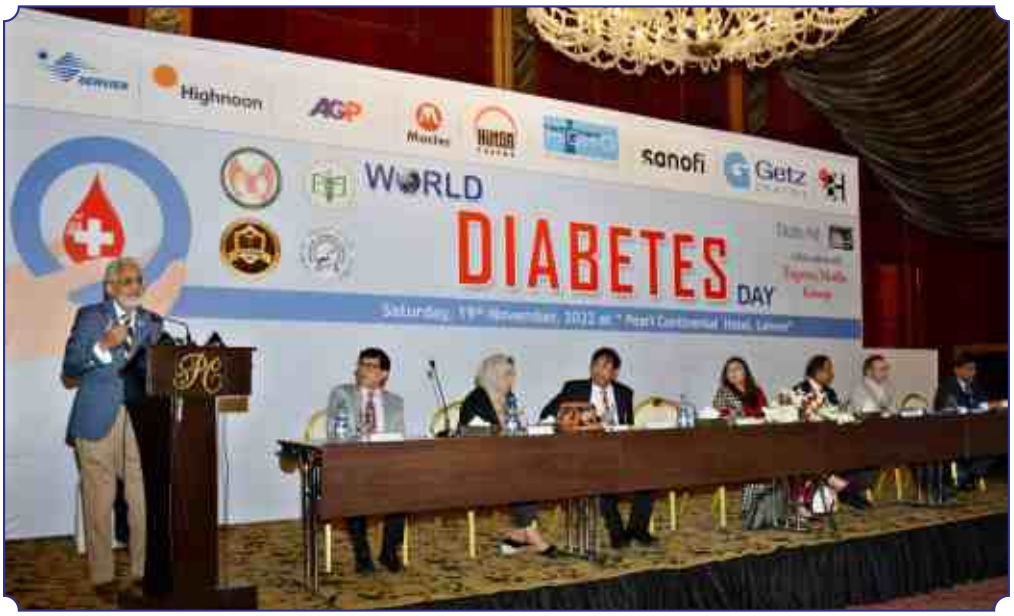
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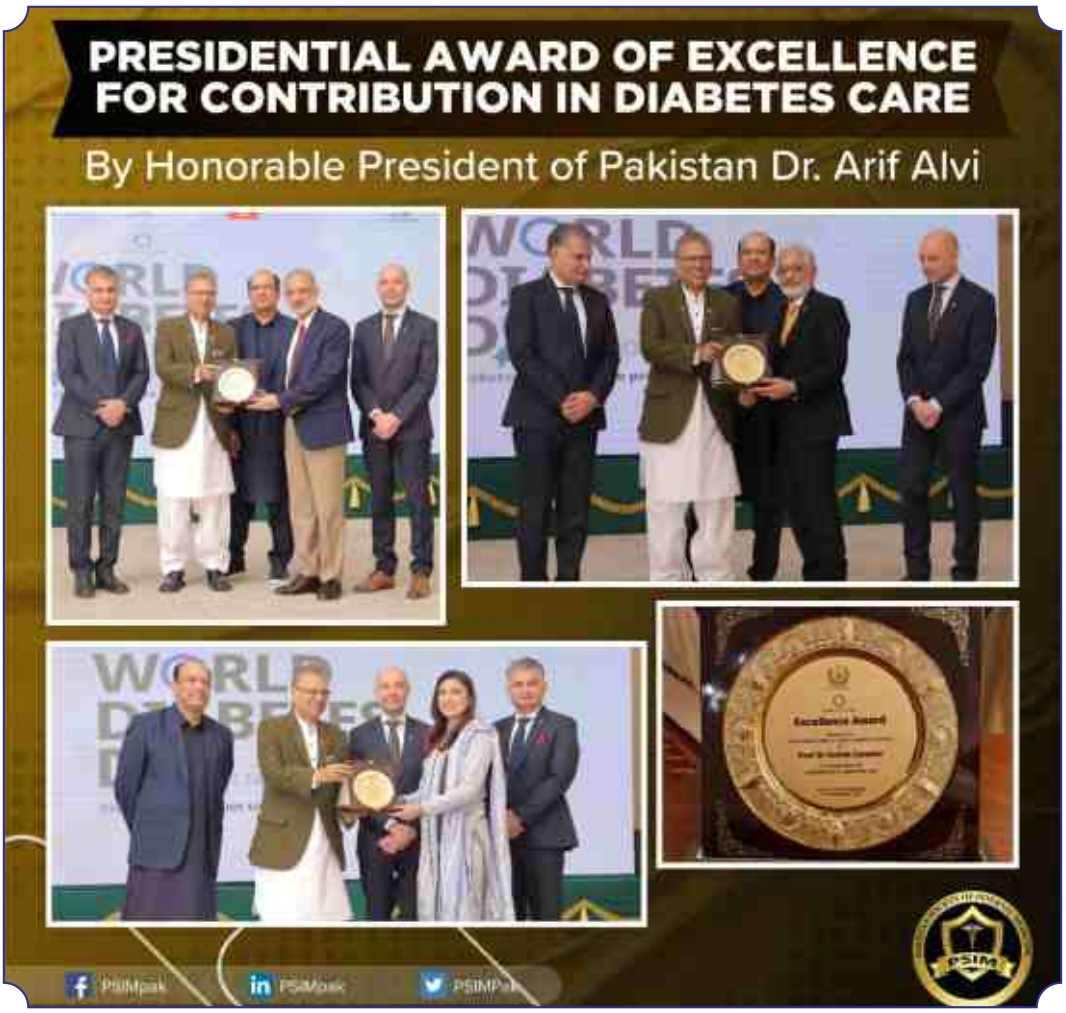
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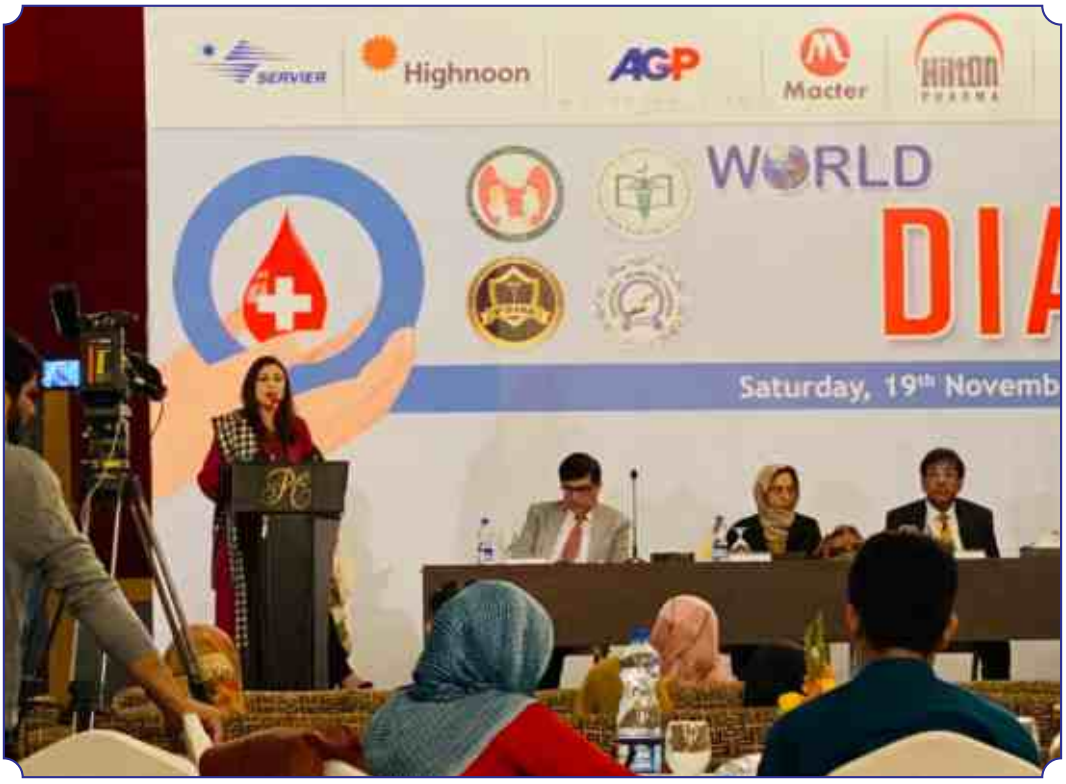
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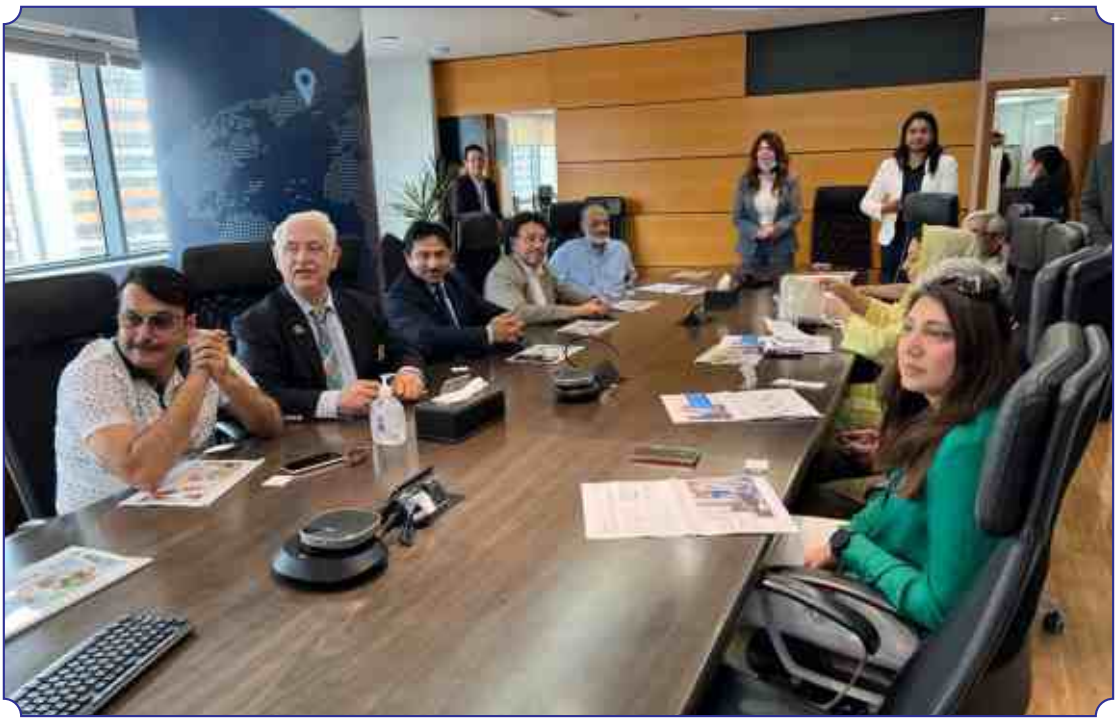

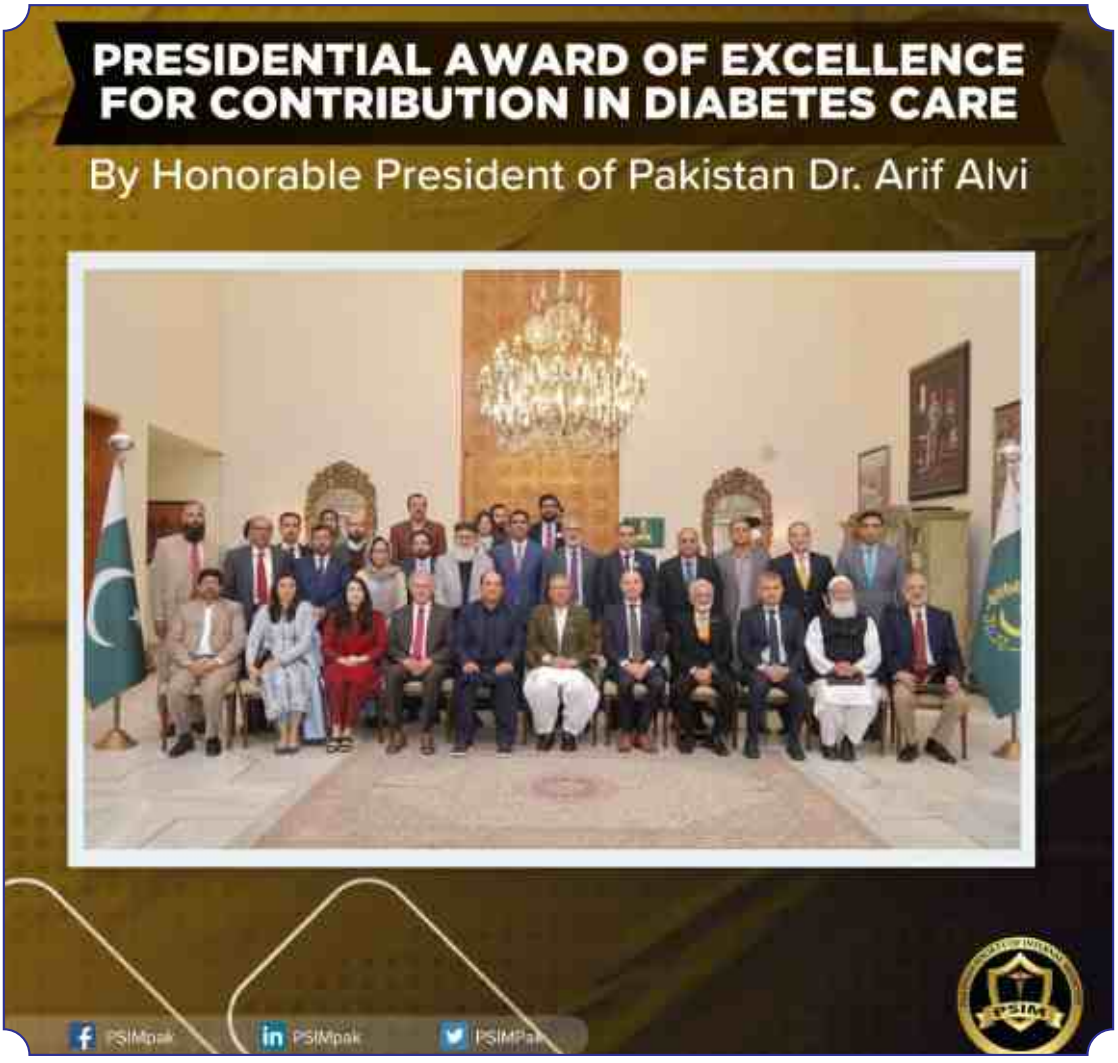
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