Editorial

Fibro-calculous pancreatic diabetes: Changing hues with changing times

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It was about four decades ago that the largest series on tropical pancreatitis from Kerala by Geeverghese brought to light the existence of a curious form of pancreatic disease which affected the young, led to diabetes and caused early death.[1] Soon there were similar reports from other parts of the world, mostly areas in the tropics making the circle of latitude, malnutrition and a few food products' attractive explanations for possible etiology of this condition.

Over the years, we have learnt that the entity occurs in areas outside of the tropics, e.g in North India, there is no parenchymal calcification; instead there are calculi, and the pathologists are absolutely sure that the inflammation is a more a reaction than a cause, almost rendering the label of tropical calcific pancreatitis a misnomer.

Much of what is understood has come out of regular comparison of notes of the various teams grappling with this entity, and the biggest step forward has been the setting up of a nationwide online pancreatitis registry, which is actively recruiting cases from over 32 centers and following up on them prospectively. The Registry published a report recently, which involved over a thousand chronic pancreatitis patients who were followed up for 18 months. The report indicates that the idiopathic variety was the most common (60%) and alcoholic the second (38.7%). Going by the Registry's diagnostic criteria of age less than 30 years, body mass index (BMI) < 18 kg/m^2, and subjects with chronic pancreatitis who did not consume alcohol or have another cause for chronic pancreatitis, only 3.6% had tropical pancreatitis.

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The most important finding has been the rising numbers of alcoholic pancreatitis and fall in the number of tropical pancreatitis. This highlights the changing profile of chronic pancreatitis possibly attributable to the increasing use of alcohol and the improved nutrition over the decades.[2]

Another large-scale report with respect to pancreatic diabetes was published recently from a diabetes care centre in Chennai. It was a retrospective analysis of all patients registered between January 1991 and December 2010, analysed in blocks of 5 years. Of the total of 1032 cases of diabetes secondary to chronic pancreatitis, fibro-calculous pancreatic diabetes (FCPD) comprised 898 (87%) and alcoholic chronic pancreatitis 134 (13%). The prevalence of FCPD amongst the total diabetic population decreased from 1.6% (371/23,788) during 1991-1995 to 0.2% (122/70,394) during 2006-2010. They reported a drop in the actual number of patients of FCPD, although the total number of patients with diabetes has increased in this centre over the 20 years. The prevalence of alcoholic pancreatitis remained constant at 0.1%. The mean age at diagnosis of FCPD has increased significantly from 32.5 years in the early nineties to 37.5 years in recent years ($P < 0.001$) and a significant increase in the BMI of FCPD patients (19.4 + 3.6 vs. 21.2 + 3.8 kg/m^2, $P < 0.001$).[3] Thus, it seems that the disease process is evolving as is our understanding of it.

The difference in the prevalence between the two studies, though one is on chronic pancreatitis and the other on FCPD, is due to the different diagnostic criteria used. The diagnostic criteria for FCPD used by the team from Chennai is more inclusive and less stringent and may be more relevant as the disease profile has evolved to involve patients who are older and have higher BMI as against the criteria used in the pancreatitis report.

The survival and prognosis for FCPD patients has changed for the better from its classical description of death in the prime of their life.[1] One study pointed out a median

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survival time of about 25 years from the time of diagnosis of FCPD.[4] This may be a result of better access to health care, more awareness amongst patients, better management of diabetes, infections and acute exacerbation of pancreatitis, and improved nutrition standards.

The most common cause of death in patients with FCPD in the aforementioned study was diabetic nephropathy. The prevalence of microvascular complications in FCPD, which are more closely aligned with hyperglycemia, is comparable with their prevalence rates in other forms of diabetes.[5]

In a study of patients with the onset of diabetes before the age of 30, peripheral neuropathy was reported to be the highest (43.5%) in FCPD as compared to other types of diabetes.[6] The prevalence of autonomic neuropathy increases with the duration of diabetes and has been reported in over 60% of FCPD patients with more than 16 years of diabetes.[7] The possible co-existing nutritional deficiencies in the malnourished FCPD patient may play a role in the worsening neurotoxicity.

Macrovascular complications have been reported, though less frequently in FCPD. Peripheral artery disease has been reported at 4.7% and coronary artery disease at 5.1%.[5] This lower prevalence in FCPD patients has been traditionally attributed to their younger age, lower BMI, and lower cholesterol levels. A recent study done at our centre has documented increased body fat percentage (bio-impedance method) in 67.7% of patients and increased insulin resistance as documented by HOMA-IR level > 2 in 77.4% of patients.[8] These findings have been echoed by an earlier report as well.[9] What might be the cause of this insulin resistance? Sarcopenia, which is a common feature in most patients of FCPD, is a likely explanation. Or are the FCPD patients slowly acquiring visceral obesity on the path of improving nutrition and thus merging into the larger mainstream pandemic of metabolic syndrome? If so, should we keep an eye out for a possible rise in macrovascular complications in the future? The presence of neuropathy might mask or alter the presentation of coronary artery disease, thereby delaying its recognition.

While it is heartening to acknowledge that the hurtling natural course of the FPCD has slowed down enough to manifest the long-term complications of diabetes, with it arises the need to monitor and treat the same earlier on, to improve the quality of life of the affected.

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