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Short Communication

The Journey of Alzheimer's Disease Diagnosis in Bangladesh and Current Perspective

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Alzheimer's disease (AD) is a devastating pathologic process that constitutes by far the leading cause of dementia. The current global estimated prevalence is as high as 26.6 million [1] and is predicted to be doubled by 2040 [2]. Since there is no effective treatment to stop or reverse the progression of disease, the affected person becomes reliant on caregivers for assistance. This translates into significant social, psychological, physical and economic burden for patients and caregivers [3,4].

With the increasing life expectancy, the prevalence of dementia is also rising at an alarming rate in Asia including Bangladesh. Dementia care has got least priority in healthcare policy in Bangladesh and most often, people living with the condition go undiagnosed or suffer from management.

Of the 35 million people currently living with dementia globally, 58 percent live in low- and middle-income countries like Bangladesh. This figure is projected to reach 71 percent of the total by 2050 while in the coming 20 years, the eastern and southern Asia will observe a dementia growth rates more than double.

Alzheimer disease is the most common cause of dementia, but it is often used as an umbrella term for several conditions (e.g. stroke, Parkinson's disease and some other neurological diseases) causing dementia. According to evidences accumulated over the last few years, early detection of AD is important because the currently available treatments would at least decelerate its progression at full blown form. Thus, mild cognitive impairment (MCI), pre-dementia stage, has become the topic of more intense medical research.

As developing countries progress in a state of transition to non-communicable diseases, AD appears to rise in importance; further straining the already overloaded health care system of many low-middle income countries [5]. Moreover, at the same time, there is a significant rise in developing countries of other non-communicable diseases, such as diabetes, hypertension, with the known associated microvascular and vascular damage that can act as an important comorbidity in patients with MCI.

Functional and structural brain imaging has been progressing rapidly. It plays a vital role in the differential diagnosis of dementia, early recognition of progressive dementia, and monitoring of disease progression and treatment effect. Computed tomography (CT) and magnetic resonance imaging (MRI) identify structural brain abnormalities that could cause cognitive impairment [6]. Structural MRI is also useful to measure the volumetric changes of the brain, especially medial temporal lobe structures in normal aging, MCI, and AD. Pathological studies find a close association between hippocampal size measured by MRI and the extent of AD pathology [7].

Additionally, the robustness of PET results in the AD diagnosis and progression could be limited by variability between centers and interpreters. As observed in a recent systematic review of the literature, the accuracy of imaging AD biomarkers is at least as dependent on how the imaging biomarker is interpreted as on the type of biomarker itself [8]. The most widely used reading tool for all imaging biomarkers (including both MRI or PET) is simple visual interpretation [9], that heavily relies on the observer experience of what is the normal pattern of the radiotracer distribution.

To overcome the limitation of qualitative image interpretation, software programs that can aid the visual reading of FDG-PET studies, (i.e. NEUROSTAT/3D-SSP [10]; single-case SPM); automated summary measures of AD-related hypometabolism like the t-sum [11], hypometabolic convergence index [12] and AD-score [13] have been developed.

Specificity of FDG-PET for diagnosis of AD at the dementia stage increases from 64% by visual reading to 83 - 90% by quantitative software interpretation. In addition, a moderate increase of positive likelihood ratio was observed when voxel based analysis methods was used in the evaluation of FDG-brain PET, while this increase is much heterogeneous for Amyloid-PET studies [14].

Clinical application of structural brain imaging started in Bangladesh since early 1980s. The era of functional brain imaging started in 1997 as Prof. Mizanul Hasan pioneered nuclear neuroimaging at National Institute of Nuclear Medicine and Allied Sciences (NINMAS) (the then Institute of Nuclear Medicine or INM) with the advent of Tc-99m HMPAO planar brain imaging. Nuclear neuroimaging techniques, however, have been used in Bangladesh for last 20 years within limited scopes of occasional planar and SPECT imaging.

A further surge in radionuclide neuroimaging has been taking place for past two years. This is mainly brought as Bangladesh has started participating in coordinated research project (CRP) of international atomic energy agency (IAEA) in the field of neuroimaging. That supported in capacity building for advanced neuroimaging using available equipments and facilities in our country. Currently we have brain SPECT, F-18 FDG brain PET CT, 3T brain MRI and Apo E genotyping facilities in our country for the diagnosis of Alzheimer's disease as well as for other neurological conditions. Application of sophisticated analysis in neuroimaging with 3D-SSP neurostat has been possible with the support from Prof. Satoshi Minoshima and IAEA. We have also been gifted with easy Z score imaging system (E ZIS) software from Prof. Hiroshi Matsuda. Thus, our standard of practice is elevated as we are regularly performing severity assessment of AD. E-ZIS allows computer assisted statistical analysis of brain perfusion SPECT images. Voxel based analysis performed by using a Z-score map calculated from comparison of patient's data with the control data base in same manner as in a 3D-SSP method. It assesses severity of regional cerebral blood flow (rCBF) decreased in a specific region of AD, extent of area of decreased rCBF and ratio of area of decreased rCBF to that of whole brain. Furthermore, ApoE genotyping available in our laboratories is aiding screening of minimal cognitive impairment. Our future plan is to incorporate amyloid PET scan and other receptor imaging in our current array.

Accurate diagnosis has important implications on therapy, prognostication and counseling of patients caregivers. There is no effective treatment that could stop or reverse the progression of AD. Experts apprehend that an early detection of AD can at least delay the evolvement with help of currently available management. The nuclear physicians of Bangladesh, with an aim to contribute to this situation, strive to achieve the global standards.

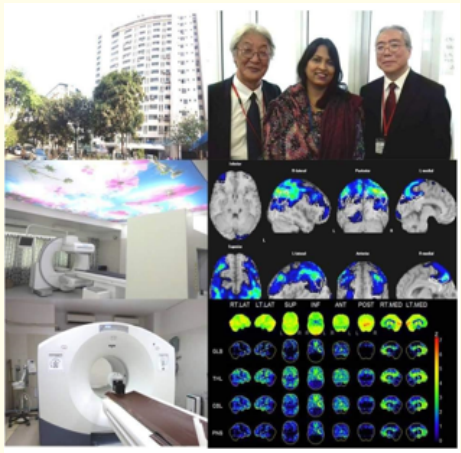

Figure 1: *Current neuroimaging facilities at NINMAS.*

Figure 2: *Historical Image of NINMAS and Prof. Mizanul Hasan.*

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