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DEMENTIA IN PAKISTAN: NATIONAL GUIDELINES FOR CLINICIANS

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INTRODUCTION

Dementia refers to a range of disorders characterized by declining memory, multiple cognitive deficits and eventual mortality due to progressive and irreversible brain damage[1]. Disease entities comprising dementia characteristically affect mainly the geriatric population. Together, they constitute a major component of global disease burden in general and geriatric disease burden in particular[2]. In 2005, it was estimated that 24.3 million people in the world were living with dementia; 4.6 million cases have been added each year ever since3. Overall, dementia contributes 11.3% of years of life lived with disability, making it a major contributor to worldwide morbidity[4].

As the world's sixth most populous country, Pakistan faces a stiff challenge of managing an aging population in the years ahead.

Table 1: Geriatric Burden in Pakistan[5, 6]

Parameter	Current	Projected
65+ Population	8 million	27 million (2050)
Old-age dependence ratio*	8.8/100	23.7/100 (2060)

***(number of 65+ individuals for every hundred working-individuals aged 20-64)**

According to the Delphi consensus study3, the prevalence of dementia in South Asia is estimated to be 1.9%. These numbers imply that presently more than 150,000 people are living with dementia in the country. Evidently, this number is anticipated to grow rapidly in the next few decades. This constitutes a looming public health as well as socioeconomic challenge that require tailored and systematic planning keeping in view the economic, cultural and healthcare paradigm that we live in.

2. PROPOSAL & METHODS

Dementia in Pakistan has so far been grossly under-studied. No population based-study has been undertaken to date and data on clinical characteristics is scarce. This makes formulation of evidence-based national guidelines a tough task. Regardless, a clinical guideline is paramount to enable efficient and proper management of patients currently under care for or presenting with dementia at primary, secondary and tertiary care facilities across the country. For this purpose, the authors used currently available tools to review relevant data on epidemiology, diagnosis, management and follow-up care of dementia as well as International guidelines published worldwide, particularly those from developing countries. Special attention was given to World Alzheimer's report 2011, Cochrane reviews, the current issue of Continuum and NICE guidelines [4, 7, 8, 9] .The authors also analyzed clinical data from their own registry of dementia patients presenting to a tertiary care center.

These guidelines are not only targeted towards local primary care physicians but will also be a useful reference at all levels of practice. An effort has been made to include only the most relevant aspects of dementia care. Annual updates will be undertaken as more relevant evidence becomes available.

3. RECOGNIZING DEMENTIA

Lack of awareness about dementia is quite common in both the general population as well as the physician workforce. The latter may be due to a lack of focus on geriatric medical education in medical schools which in turn leaves medical practices to be dictated by personal and cultural experiences[10].Detection of differences between normal aging and dementia then becomes rather difficult for the non-discerning eye. Differences usually elicited by a thorough history at the primary care level are listed the table 2 below[11].

Table 2: Clinical differences between normal aging and Dementia

NORMAL AGING	DEMENTIA
Independent in all activities of daily living (ADL)	Dependent on others for ADL
Patient claims of memory loss but can recall incidents of forgetfulness	May report memory loss if asked, unable to recall instances of forgetfulness
Patient more concerned about memory loss	Close family members more concerned about memory loss
Recent memory of events and conversations intact	Notable decline in memory of recent events and conversations
Occasional difficulty in finding words (expressive aphasia)	Frequently experiences difficulty in finding words with or without difficulty of understanding (expressive and receptive aphasia)
No history of getting lost in familiar territory, may pause briefly to reorient	History of getting lost in familiar territory while walking or driving
Able to operate common appliances	Unable to operate common appliances
Normal interpersonal and social skills	Loss of interpersonal and social skills, lack of interest in social activities or inappropriate behavior

Due to lack of awareness in the general population, caregivers are highly likely to mistake dementia for age-related cognitive decline and fail to report it to doctors [12, 13]. Due to small number of specialist physicians and limited access to specialist care, primary care physicians (PCP) should play key role in the recognition, diagnosis, and management of patients with dementia.

RECOMMENDATION

- PCPs should learn how to assess patients with early signs of dementia.
- A focused history concerning mental function should be undertaken during all geriatric outpatient visits to aid early detection, diagnosis and symptomatic relief.
- Seminars, workshops and public awareness sessions should be arranged to increase awareness about dementia and its impact on physical and social functioning

4. DIAGNOSING DEMENTIA

The DSM IV definition of dementia is comprehensive and is widely acceptable for making a diagnosis of dementia. The development of multiple cognitive deficits that include memory impairment and at least one of the following: aphasia, apraxia, agnosia, or a disturbance in executive functioning. These deficits must be sufficiently severe to cause impairment in occupational or social functioning and must represent a decline from a previously higher level of functioning [14].

Once a possible diagnosis of dementia is suspected on history, a full cognitive, mental, medical and physical evaluation should be undertaken.

Clinical cognitive examination of attention and concentration, orientation, short and long-term memory, praxis, language and executive function can be accomplished using a standardized instrument like MMSE. Urdu translations of MMSE are currently undergoing validation. Interpreting MMSE score should take in to account factors known to affect performance, including educational level, skills, prior level of functioning, language, any sensory impairments, psychiatric illness or physical/neurological problems9. A score ?26 is usually considered normal, a score of 20-25 indicates mild, 10-19 moderate and < 10 severe dementia (Table 3). Another screening tool that can

Table 3. Stages and Progression of Dementia

Stages	Symptoms
Preclinical :	No symptoms. This stage of Alzheimer's can last for years, possibly even decades. New imaging technologies and biomarkers may detect disease during this stage.
Mild cognitive impairment (MCI) : Score > or = 26	Mild changes in their memory and thinking ability but changes MMSE not significant enough to affect work or relationships yet. May have memory lapses, problems with judgment and time
	management and decision making.
Mild dementia: MMSE Score: 20-25	Alzheimer's disease is often diagnosed in the mild dementia stage, when there is significant trouble with memory, thinking, organizing, expression, problem-solving, complex tasks and sound judgments. Changes in personality. Getting lost or misplacing belongings
Moderate dementia MMSE Score: 10-19	Poor judgment and deepening confusion, loss of orientation of place, time and person. Greater memory loss, forget their address or phone number, personal belongings. They repeat favorite stories or make up stories. Need help with some daily activities and develop incontinence of urine and bowels. Significant changes in personality and behavior. May hallucinate and become restless or agitated.
Severe dementia MMSE Score: < 10	Further decline in cognitive and phys ical capabilities. Lose the ability to communicate or speak coherently. Require daily assistance with personal care, eating, dressing, walking and toileting. Later, there is loss of swallowing and control of bladder and bowels, ultimately leading to a bedbound vegetative state.

be used is Mini-Cognitive Assessment tool (Mini-Cog) with the same sensitivity and specificity as that of MMSE. Montreal Cognitive Assessment (MoCA) assesses multiple cognitive domains and has low susceptibility to educational and cultural bias. Ascertain Dementia (AD8) is an informant based screening tool that assesses memory, orientation, function and judgment. Use of AD8 can improve detection of dementia in primary setting to 97% for dementia and 91% for MCI. Daily functional assessment of patients can be done by interviewing and using ADL scale. More advance functioning like shopping, managing finances can be assessed by instrumental ADLs (IADLs). Functional Assessment Questionnaire (FAQ) can also be used to assess more complex activities.

Neuropsychiatric evaluation should be conducted for detection of coexisting depression, psychosis, agitation and other complaints. The Neuropsychiatric Inventory Questionnaire (NPI-Q) is a quickly administered instrument that provides reliable assessment of behaviors commonly observed in patients with dementia. Investigations warranted to rule out medical causes of cognitive impairment include serum electrolytes, calcium, magnesium, phosphate, glucose, liver & renal function tests, TSH, B12 and folate levels. Cognitive impairment of acute onset in the setting of medical illness is suggestive of delirium and should be ruled out as well. Neuroimaging should be performed in the diagnostic work up to exclude other potentially treatable causes of dementia, to look for vascular lesions and to differentiate different types of dementia. MRI is preferable over CT brain. For rapidly progressive dementia the MRI should include DWI and ADC sequence. Functional imaging is recommended only in cases where diagnosis is in doubt after clinical and structural imaging and in special circumstances[15]

Routine medications known to cause memory impairmen11 should be accounted for. These include anti-histamines (both H1 & H2 blockers), Digoxin, anti-cholinergics, anti-convulsants (phenytoin, valproic acid, carbamazepine), tricyclic antidepressants, beta-blockers, alpha-blockers, calchium-channel blockers, Lithium, typical anti-psychotics and anti-Parkinsonian agents (L-dopa, pergolide, bromocriptine)

RECOMMENDATIONS

- For cognitive assessment screening tools like MMSE, Mini-Cog should be used. If MMSE is used, the educational background of the patient should be documented as well for accurate interpretation of MMSE.
- Common treatable causes of memory loss like vitamin B12 deficiency, hypothyroidism and normal pressure hydrocephalus should be ruled out.
- Neuro-imaging, preferably an MRI of the brain should be done in order to reach a reasonably accurate diagnosis. For rapidly progressive dementia the MRI should include DWI and ADC sequences.

5. DIFFERENTIATING DEMENTIA

Features of different disease entities comprising dementia are listed in Table 4.

Table 4: Major disease entities comprising dementia are listed. All diagnoses of dementia require that deficits must represent a decline from previous function and must lead to impairment in performing ADLs. Other causes that may account for these symptoms must always be excluded first.

Disease (Criteria Source)	Diagnostic Criteria
Alzheimer's (DSM-IV)	Objectively demonstrated memory deficit PLUS at least one of the following: Aphasia (abnormal speech) Executive function impairment (difficulty planning, judgment, abstraction, problem-solving etc) Agnosia (impaired recognition of people or objects) Apraxia (impaired performance of learned motor skills) Clinical features: Symptomatic course is gradual and progressive.

Vascular Dementia (NINDS – AIREN)	Focal neurological signs on exams consistent with stroke AND evidence of CVD on brain imaging (CT or MRI) PLUS at least one of the following: Onset of dementia within 3 months following a recognized stroke Abrupt deterioration in cognitive function Stepwise progression of cognitive deficit Clinical features: early presence of gait disturbance; history of unsteadiness and frequent, unprovoked falls; early urinary frequency, urgency, and other urinary symptoms not explained by urologic disease; pseudo-bulbar palsy; personality and mood changes, abulia, depression, emotional incontinence, or other subcortical deficits including psychomotor retardation
Lewy Body (ICC for DLB)	Two of the following are required for a diagnosis of probable Dementia with Lewy bodies: Fluctuating cognition with pronounced variations in attention and alertness Recurrent visual hallucinations which are typically well-formed and detailed Spontaneous motor features of Parkinsonism Clinical features: Prominent deficits in attention, visuospatial ability and fronto-subcortical skills; history of falls & syncope; systematized delusions and hallucinations worsened by neuroleptics
Fronto-Temporal Dementia (Lund-Manchester)	ALL of the following must be present: Insidious onset and gradual progression Early decline in social interpersonal conduct Early impairment in regulation of personal conduct Early emotional blunting Early loss of insight
	Clinical features: Usually presents in middle-age with behavioral, speech, personality and conduct issues. Memory is often minimally impaired early on. Frontal lobe signs including primitive reflexes, akinesia and incontinence may be evident
Parkinson's Dementia (EMRE et al)	Core criteria: Previously diagnosed Parkinson's disease presenting with dementia. Supportive features: Typical profile of cognitive impairment plus behavioral symptoms including apathy, depressed or anxious mood, hallucinations, delusions, excessive daytime sleepiness etc).
Normal Pressure Hydrocephalus	Triad of gait disturbance, urinary complaints and cognitive impairment should raise suspicion of NPH. Early cognitive deficits include psychomotor slowing, impaired attention and executive & visuospatial dysfunction.
Crautzfeldt-Jacob Disease (MRI-CJD Consortium)	Rapidly progressive dementia AND at least two out of the following four clinical features: Myoclonus Visual or Cerebellar signs Pyramidal/extrapyramidal signs Akinetic mutism
	AND a positive result on at least one of the following laboratory tests: Typical EEG (periodic sharp wave complexes) during an illness of any duration; and/or Positive 14-3-3 CSF assay in patients with a disease duration of less than 2 years MRI high signal abnormalities in caudate nucleus and/or putamen on DWI or FLAIR sequence
Mixed Type	Hallmark abnormalities of Alzheimer's along with features of others, most commonly Vascular and Lewy Body dementias. Note that Alzheimer's should not be diagnosed in the presence of evidence of significant CVD

6. MANAGING DEMENTIA

6.1. Pharmacological management

6.1.1. Symptomatic Treatment

Although studies suggest a small degree of benefit clinically, cholinesterase inhibitors should be considered in patients with mild to moderate Alzheimer's. In three double-blind placebo-controlled trials, donepezil produced a significant improvement lasting 3 to 6 months on both a composite test and a clinician's global evaluation in individuals with both Alzheimer's & vascular dementia. Efficacy has been demonstrated at doses of both 5 and 10 mg; a5 mg QD dose can be increased to 10 mg QD after 4 to 6 weeks. Side effects occurred in up to 17% of subjects exposed to the drug. Six studies have reported a dose-response effect with increasing frequency of adverse events as dosage [16, 17, 18, 19, 20, 21]. Nine adverse events had statistically significant effect sizes in patients with Alzheimer disease; diarrhea (relative risk, 2.57) and nausea (relative risk, 2.54) were reported most frequently. For patients with vascular dementia, abnormal dreams, diarrhea, nausea, and muscle and leg cramps were statistically significant; muscle cramps had the largest effect size (relative risk, 9.62), and nausea had the smallest (relative risk, 2.21).

Treatment with rivastigmine for 6 months resulted in significant differences compared with placebo in cognition and on a clinician's global assessment and an activities of daily living scale[22, 23, 24]. Higher doses (6 to 12 mg per day) yielded better outcomes than lower doses (1 to 4 mg per day), which were no better than placebo in one study. Side effects (including weight loss) were present in up to half of those in higher-dose groups and led to discontinuation of the drug in up to a quarter. The initial dose is 1.5 mg BID, which can be increased to 3 mg BID, then 4.5 mg BID, then 6 mg BID with a minimum of 2 weeks intervening period between increases. The rivastigmine transdermal patch formulation when compared to the rivastigmine capsule showed a less fluctuating and a more continuous drug delivery and improved tolerability [25]. Another study of the 9.5 cm2 Rivastigmine patch showed similar efficacy to capsules 6mg BID) with approximately two-thirds fewer reports of nausea and vomiting26. Recently a 13.3mg rivatigmin transdermal patch has been approved by FDA[27]

Galantamine was tested in more than 1,600 subjects with mild to moderate AD in two double-blind, placebo-controlled studies. Treatment with galantamine (16 to 32 mg per day) resulted in significant cognitive improvement on the Alzheimer's disease Assessment Scale-Cognitive Subscale (ADAS-Cog), a clinician's global assessment, theactivities of daily living scale, and a behavior scale. Efficacy was present at 16 mg/day and 24 mg/day. Side effects occurred in up to 13% at 16 mg per day and up to 17% of subjects exposed to 24 mg per day.[28, 29] Memantine, an NMDA receptor antagonist, improved cognition and global functioning in two poorly defined groups of patients with dementia.[30, 31]

A pooled estimate from 3 trials showed that 20 mg/d memantine resulted in statistically significant improvement on the ADAS-cog scale in cognition for individuals with mild to moderate vascular dementia [32,33] and mild to moderate Alzheimer disease[34]. In addition, patients with moderate to severe Alzheimer disease showed statistically significant improvement on the SIB scale [35, 36]. However, patients with mixed dementia had no difference[37]. Three of four studies that evaluated quality of life found statistically significant improvements, and the summary estimate was statistically significant. Two trials evaluated caregiver burden and resource utilization and found statistically significant improvements on both parameters. Two of the 6 eligible studies reported information on the proportion of patients who had a clinically important improvement on memantine. Only one of these trials reported statistical significance, and that trial did not find a statistically significant change.

The withdrawal rates related to adverse effects from memantine including nausea, dizziness, diarrhea, and agitation varied from 9% to 12% in the treatment group (7% to 13% in the placebo group).

COMPARATIVE EFFECTIVENESS

DONEPEZIL VERSUS GALANTAMINE

Two studies compared donepezil (10 mg/d) with galantamine [38, 39], focusing on Alzheimer disease, with one describing severity of dementia as mild to moderate. The results from the longer study (52 weeks) showed no statistical differences in the primary outcome of function. However, changes in secondary outcomes of cognition (measured with the ADAS-cog and MMSE) showed statistical differences favoring galantamine in patients with MMSE scores between 12 and 18 only. The most frequently reported adverse events were nausea, agitation, vomiting, headache, and falls. The rates for adverse events were marginally higher for galantamine but were not statistically evaluated. Serious

adverse events did not differ between galantamine and donepezil.

DONEPEZIL VERSUS RIVASTIGMINE

One large trial compared donepezil (up to 10 mg/d for 2 years) with rivastigmine (up to 12 mg/d for 2 years) and focused on patients with moderately severe Alzheimer disease for more than 2 years [40, 41] .The results statistically significantly differed in global function (Global Deterioration Scale) and function (Alzheimer disease Co-operative Study-Activities of Daily Living Scale), favoring rivastigmine. A subgroup analysis of patients age 75 years or older versus those younger than 75 years showed statistical differences in some measures of behavior and function, favoring rivastigmine. Comparison of adverse events showed that rivastigmine had higher rates of nausea during titration and maintenance phases. In general, patients receiving rivastigmine reported more adverse events than those receiving donepezil, but no differences in serious events were observed.

COMBINING MEMANTINE WITH A CHOLINESTERASE INHIBITOR

In one study, addition of NMDA receptor antagonist memantine to cholinesterase inhibitors (tacrine, donepezil, rivastigmine and galantamine) delayed admission to nursing home [42]. A systemic review [43].comparing the efficacy of acetyl cholinesterase inhibitor (aChEI) monotherapy with combination of memantine and aChEI therapy in moderate to severe AD showed a small benefit at 6 months.

6.2. NON-PHARMACOLOGICAL TREATMENT/DIETARY SUPPLEMENTS VITAMIN E, FOLATE AND OTHER NUTRIENTS

In one large, 2-year trial, selegiline (5 mg BID) and vitamin E (1,000 I.U. [alpha-tocopherol] BID) significantly delayed the time to a composite outcome of primary measures indicative of clinical worsening, and fewer patients treated with vitamin E were institutionalized44 Importantly, however, there was no additive effect from selegiline plus vitamin E, neither agent improved cognitive function (ADAS-Cog) compared with baseline values, and those on drug did not decline less than those on placebo on these types of measures. Similarly there are no clinical trials to support a recommendation of dietary and supplemental omega-3 polyunsat urated fatty acid for the sole purpose of preventing cognitive impairment or dementia.[45]

There is one ongoing phase II trial in moderate to severe dementia to determine benefit of curcumin (found in turmeric) in slowing cognitive deterioration.[46] Several studies have also showed possible link between vitamin D deficiency and cognitive decline. However further trials are needed to establish a casual relationship.[47, 48]

Trials evaluating extracts of the leaves of the maidenhair tree, Ginkgo biloba, that has been used in China for long time for cognitive impairment have shown conflicting results and Chochrane review has concluded that the benefits of Ginkgo biloba in memory impairment are inconsistent49. Similar conclusions have been drawn for ginseng[50], hydergine[51] and piracetam[52]. The World Alzheimer Report 2011 [53] in its comprehensive analysis of the Cochrane systemic review concluded that there is no evidence to recommend the use of nutritional supplements at any stage of dementia

RECOMMENDATIONS

- The decision to initiate a trial of therapy with a cholinesterase inhibitor or memantine should be made by the treating physician based on individualized assessment.
- Cholinesterase inhibitors are recommended for mild to moderate disease. No specific cholinesterase inhibitor is recommended over another.
- Memantine and donepezil is recommended for moderate to severe disease. Combination therapy was also found to be safe and tolerable in moderate to severe disease
- At present there is no evidence that support the use of ginkgo biloba, ginseng, hydergine and piracetam in the treatment of dementia
- Presently the evidence does not support the use of nutritional suppliments for the treatment of dementia

6.3. PSYCHOLOGICAL AND BEHAVIORAL ISSUES IN DEMENTIA

The most common behavioral symptoms are agitation, aggression, depression, apathy, psychosis and hallucinations, which are more disturbing to family and care givers than memory disturbances. Common triggers are pain, fecal impaction, acute medical illness, boredom, loneliness, depression, and social and environmental stressors.

6.3.1. NON-PHARMACOLOGICAL INTERVENTIONS

Non-pharmacological interventions include redirecting

and refocusing the patient, increasing social interaction, initiating enjoyable activities, establishing regular sleep habits, eliminating sources of conflict and frustration, and establishing rewards for successes.[54] Cognitive behavioral therapy may help clinician understand patient's needs and thus tailor the treatment accordingly.[55]

6.3.2. PHARMACOLOGICAL MANAGEMENT

Pharmacological treatment is required when patient does not respond to non-pharmacological interventions. Commonly used agents are antipsychotics both typical and atypical, antidepressants and mood stabilizing agents. A metaanalysis of 3353 patients randomized to study drug showed a 50% increase in risk of death from all causes with no difference in risk in the studied agents. It is recommended that drugs should only be used when non pharmacological interventions fail to improve symptoms.[56]

Tricyclic antidepressants and benzodiazepines are generally avoided in patients with dementia.[57] Low dose trazodone, carbamezapine, valproate and SSRIs like citalopram are found to be effective in treatment of agitation[58]. Selective serotonin inhibitors (SSRIs) are also found to be effective in the treatment of depression.[59]

RECOMMENDATIONS

- Non pharmacological interventions should be tried first for the management of psychological and behavior issues in patients with dementia
- Atypical antipsychotics, low dose trazodone, valproate, carbamezapine and SSRIs can be used in the treatment of agitation and other psychological issues

1. PATIENT SAFETY ISSUES

Patient safety should be assessed and any gap should be addressed on follow up visits for all dementia patients. Common safety issues that can lead to significant morbidity and even mortality are presence of sharp object within easy reach, slippery floor, loose throw rugs, poor lighting etc. Driving is contraindicated for demented patients as they have poor reasoning and safety awareness as well as impaired ADLs and instrumental activities of daily living (IADL).

2. ADVANCE DIRECTIVES AND WILL

When the diagnosis of dementia is made and disclosed to the patient and family it is also important to discuss issues of advance directives and the patient should update his or her will before the patient loses his capacity to disclose his or her wishes on these matters.

3. GENETICS AND GENETIC TESTING OF ALZHEIMERS DISEASE AND FRONTAL LOBE DEGENERATION

Advancements in neurogenetics have led to identification of several genes for Alzheimers disease. These include mutations in the Amyloid Precursor protein gene (APP gene) and mutations in the Presenilin 1 gene (PSEN1) which are the most common cause of Familial AD. The PSEN1 mutations tend to cause young onset AD. Mutations in the Presenilin 2 gene are rare and tend to cause the older onset of disease. Apolipoprotein E (Apo E) is a protein involved in lipid transport and its prevalence in individuals with AD is around 50%, whereas in the general population its prevalence ranges from 15%-20%.60 Individuals with two copies of Apo E4 increase the risk of younger onset AD. The prevalence of Apo E4 gene in our population is unknown. As there is no cure or prophylaxis for AD, genetic testing for AD is not routinely recommended. The same goes for biomarker testing in normal individuals with a family history of AD, since a positive test may lead to psychological issues and distress. Three genes have been mainly found to be responsible for Frontotemporal lobe degeneration (FTD). Two genes, both located on 17q21: the microtubule associated protein tau (MAPT) and the progranulin (GRN) genes are responsible for 10%-20% of cases of familial FTD. Recently in 2012 two groups simultaneously published the discovery of another gene; a hexanucleotide repeat expansion in Chromosome 9p (CRORF72) in families with FTD and amyotrophic lateral sclerosis (ALS).61,62 Similarly for the same reasons as in AD, genetic testing for FTD should not be contemplated without genetic counseling.

RECOMMENDATION

- Genetic testing for normal individuals with a family history of AD or FTD is not routinely recommended due to unavailability of disease modifying treatment and the psychological stress and distress it may cause.

4. CAREGIVER STRESS AND DISTRESS

Caregivers of patients with dementia often suffer from depression and long term social support to them help improve their symptoms.63 Our own study (unpublished data) showed that 123 out of 125(98.4%) primary

caregivers reported some level of distress. So, caregiver distress is a prevalent problem in our setting and is significantly dependent on the behavioral and psychiatric symptoms of dementia

RECOMMENDATION

- Care givers should be given assistance and guidance in care giving and periodic assessment of their own health should be performed.

5. MILD COGNITIVE IMPAIRMENT

Having discussed all aspects of dementia pertinent to our population, it is worth mentioning that when measurable criteria for dementia(e.g. MMSE) are not met, yet the patient complains of progressive cognitive decline without impairment of ADL's, the term mild cognitive impairment(MCI) may be used (Table 3). This group encompasses patients who later on would progress to dementia, especially AD and also those suffering from psychiatric disorders (pseudo-dementia), systemic illness or senility, who do not progress to dementia. The most acceptable criteria for MCI includes four subgroups; (a) deficits in memory alone, (b) deficits in memory plus deficits in another cognitive domain, (c) deficits in a single non memory domain and (d) deficits in more than one non-memory domains.64,65 To date, there is no consensus on the pharmacological or non pharmacological treatment of MCI.[66]

6. RECOMMENDATIONS (SUMMARY)

- The DSM IV definition of dementia should be used for diagnostic purposes
- An attempt should be made to identify the type of dementia.
- A cognitive evaluation should be done and documented. We recommend MMSE either English or Urdu version. The educational background of the patient should be documented as well for accurate interpretation of MMSE.
- Common treatable causes of memory loss like vitamin B12 deficiency, hypothyroidism and normal pressure hydrocephalus should be ruled out.
- Neuro-imaging, preferably an MRI of the brain should be done in order to reach a reasonable diagnosis. For rapidly progressive dementia the MRI should include DWI and ADC sequences.
- The diagnosis, prognosis, quality of life issues and the absence of any disease modifying treatment should be explained to the caregivers.
- The decision to initiate a trial of therapy with a cholinesterase inhibitor or memantine should be made by the treating physician based on individualized assessment.
- The choice of pharmacologic agents should be based on tolerability, adverse effect profile, ease of use, and cost of medication. The evidence is insufficient to compare the effectiveness of different pharmacologic agents or their combinations, for the treatment of dementia.
- Genetic testing for AD and FTD in normal individuals/family members of affected patients is not routinely recommended

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