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What About Alzheimer's Disease And Other Dementias In Algeria?

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Abstract
Worldwide, the aging of the population is accelerating, with an increase in the number of people suffering from age-related illnesses. The prevalence of dementia in general and Alzheimer's disease in particular, is consequently on the rise. The World Alzheimer's Report estimated the number of people with dementia worldwide at 55.2 million in 2019.
In Algeria today, almost 8.9% of the population is over 60. This aging of the Algerian population is accompanied by an increase in the incidence of dementia, which is likely to represent a huge public health challenge. The epidemiological study carried out by the neurology department of CHU Mustapha, Algiers Centre, estimated the number of people suffering from dementia in Algeria in 2016 at 189,182 cases, including 135,849 cases of Alzheimer's disease.
Keywords: *Dementia, Alzheimer, incidence*

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I. Introduction

The world's population is aging: there are almost 900 million people aged 60 and over living in the world [1]. This aging process is occurring more rapidly in middle- and low-income countries than in high-income countries. By 2020, it is estimated that 2/3 of people over 60 will live in developing countries [2]. Increased life expectancy is contributing to the rapid rise in these numbers, and is associated with an increased prevalence of chronic diseases such as dementia.

History of the term dementia:

The term "dementia" underwent a long semantic evolution before arriving at its current meaning. It seems that Galen, in the 2nd century AD, introduced the term "dementia" ("de", out of; "mens", mind) to designate stable conditions of mental impairment.

In 1907, Alois Alzheimer published an anatomical and clinical analysis of a 51-year-old patient (Auguste Deter) who died after a progressive worsening of dementia. A histological study showed the existence of intraneuronal conglomerates of abnormal fibers coexisting with senile plaques. He gave this first complete histological description of dementia the name neurofibrillary degeneration.

But it was Kraepelin who coined the term "Alzheimer's disease" in his influential "Traité de Psychiatrie," individualizing "Alzheimer's disease" as a rare dementia of degenerative origin in young subjects, which he separated from the much more common "senile dementia," to which he attributed an atherosclerotic vascular cause.

It wasn't until the 1980s that the pathological nature of dementia in the elderly was clearly affirmed, and that in fact the majority of "senile dementias" were clinically and neuropathologically indistinguishable from "presenile Alzheimer's dementias" [3]. Alzheimer's disease now encompassed both early-onset forms in the young, often of genetic origin, and forms in the elderly, mostly sporadic.

Definition of dementia:

The American Psychiatric Association (APA) definition is the most widely used, both clinically and epidemiologically, thanks to the application of the Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnostic criteria for dementia.

In the fourth revised version of the DSM (DSM-IV TR) [4], dementia is characterized by "the onset of multiple cognitive deficits that include impaired memory and at least one of the following cognitive disturbances: aphasia, apraxia, agnosia, or disturbance of executive functions. Cognitive deficits must be sufficiently severe to cause significant impairment of occupational or social functioning, and must represent a decline from previous levels of functioning.

In 2013, the fifth version of the DSM (DSM-V) was published [5]. Modifications from DSM-IV include a change in nomenclature from dementia to major neurocognitive disorder (MNCD); the diagnosis of MNCD no longer necessarily requires memory to be one of the affected domains; and it allows for cognitive deficits limited to a single domain.

II. Classification Of Dementias

Dementias are classified according to broad nosological frameworks [3].
❖Curable dementias.
❖Degenerative dementias, particularly Alzheimer's disease (AD).
❖Vascular dementias.
❖The combination of AD and cerebrovascular disease.
❖Dementias are caused by transmissible agents (Creutzfeldt-Jakob disease).

Curable" dementias:

This term is currently considered inappropriate, and it's better to prefer "potentially curable dementias," as it's a fact that truly curable causes appear to be very rare, not to say exceptional.

There are four main etiological frameworks:
- toxic or deficiency causes: chronic ethylism, drug intoxication, vitamin deficiencies (B1, B12, folates, PP. .),
- neurosurgical" causes: brain tumors, normal-pressure hydrocephalus, chronic subdural hematoma, etc. ..;
- metabolic and endocrine causes: hypothyroidism, ...
-inflammatory or infectious causes: such as multiple sclerosis, systemic diseases, Whipple's disease, neurosyphilis and, HIV encephalitis. ...

Other non-degenerative, non-vascular dementias:
- paraneoplastic syndromes
- post-traumatic syndromes.

Degenerative dementias:
These are caused by degeneration of the brain's nerve cells. The main types are:
- Alzheimer's-type dementia,
- Dementia with focal atrophy:
- fronto-temporal lobar atrophies:
- fronto-temporal dementia,
- primary progressive aphasia,
- posterior cortical atrophy: Benson syndrome
- Striatal dementias:
- Lewy body dementias,
- Parkinson's dementias,
- progressive supranuclear palsy (PSP),
- corticobasal degeneration **(CBD),**
- Huntington's chorea...

Creutzfeldt-Jakob disease:
This is a rare, currently incurable dementia that belongs to the group of prion diseases.

III. Alzheimer's Disease (AD)

Alzheimer's disease (AD) is the most prevalent cause of dementia. It accounts for 70% of dementia cases diagnosed worldwide [6].

Neuropathology:

AD is a neurodegenerative disease characterized by two types of lesions: the progressive accumulation of extracellular amyloid plaques and intracellular neurofibrillary deposits, mainly in brain regions involved in learning and memory, but also in emotional behavior [7].

The main component of amyloid plaques is the insoluble peptide amyloid beta (AB). This neurotoxic hydrophobic peptide is derived from the enzymatic cleavage of the transmembrane protein amyloid precursor protein (APP) by the action of two enzymes, a B-secretase and an Y-secretase.

This peptide exists in two forms, one containing 40 amino acids (AB40) and another containing 42 amino acids (AB42). The latter is the form most prone to oligomerization and fibril formation, the origin of senile plaques (Figure 1).

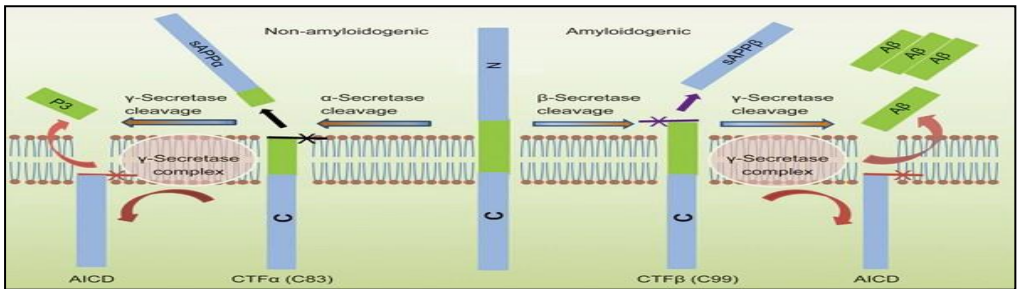

Figure 1: Formation of amyloid plaques in Alzheimer's disease [8].

The second main neuropathological feature of AD is neurofibrillary degeneration, more specifically the formation of helical filament pairs (HFPs), intraneuronal structures formed from the hyperphosphorylation of the Tau protein.

Tau is a cytosolic protein involved in the assembly of microtubules forming the cytoskeleton of neurons, a structure that ensures both the architecture and function of the neuron. Hyperphosphorylation of Tau protein affects its ability to bind to cytoskeletal microtubules, which eventually disassemble, leading Tau proteins to assemble together to form aggregates such as PHFs [9]. These PHFs accumulate in the cell bodies of neurons, producing neurofibrillary tangles.

The number and location of these tangles have been correlated with the degree of severity of dementia, whereas this has not been shown for senile plaques. However, they are thought to form after the onset of amyloid deposits [9].

Stages of Alzheimer's disease:

There is considerable inter-individual variability in the progression of Alzheimer's disease-related disorders. In Alzheimer's disease, disorders are insidious and progressive in onset. From the onset of the first symptoms, the disease evolves over a period of around ten years. Its evolution is characterized by different stages: preclinical, predementia, dementia, and finally advanced dementia.

Phase 1, the preclinical stage:

This extends over 10 to 20 years. It is an undetectable phase during which lesions gradually form. At this stage, there are as yet no clinical signs [10].

Phase 2, the pre-dementia stage

This phase takes place over a period of around 5 years, during which the first clinical signs appear. In 75% of cases, they concern problems with memory of recent events, particularly episodic memory [11]. Emotional changes may also appear. At this stage, the patient's autonomy is still preserved.

Phase 3, the dementia stage

This period lasts from 3 to 10 years on average. Initial memory problems worsen, with the onset of semantic and long-term memory disorders, as well as other deficits. Patients gradually lose their autonomy. Cognitive impairments include disorders of executive function, temporospatial orientation, language (aphasia, lack of words, paraphasias, echolalia, comprehension difficulties, dysorthographia, etc.), praxis (difficulty in linking a logical sequence of gestures with a purpose, etc.), and gnosis (difficulty in recognizing objects and using them, identifying people, etc.).

Psycho-behavioral disorders may appear, notably depression, anxiety disorders (agitation, aggressiveness, etc.), psychotic disorders (delusions, etc.), basic conduct disorders (eating disorders, weight loss, sphincter incontinence, etc.), sleep-wake rhythm disorders (inversion of the nycthemeral cycle, insomnia, etc.), stereotyped behavior and a tendency to wander.

Phase 4, the advanced dementia stage:

The picture evolves towards complete loss of autonomy, bladder and bowel control, and severe eating and swallowing difficulties. Behavioral and comprehension problems become more pronounced, and unusual behaviour is observed in public. Patients no longer recognize their immediate environment or familiar

surroundings. They have severe difficulty walking, moving around in wheelchairs, and they may become bedridden.
Neurological signs may include epileptic seizures and myoclonus.
Their general condition may rapidly deteriorate, leading to cachexia and death.

Diagnosis:

AD has been defined as a type of dementia since the publication of the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) in 1984 [12], which proposed clinical criteria for the diagnosis of AD. These criteria were applicable only when AD had reached the threshold of dementia. Even then, the diagnosis could only be considered probable at best, as certainty of diagnosis could only be provided following a post-mortem brain autopsy.

Today, specific biomarkers of AD have been identified and are available for research, with clinical use tending to become more widespread. These include morphological imaging markers (magnetic resonance imaging (MRI), hippocampal volumetry), functional imaging markers (positron emission tomography (PET) with Pittsburg Compound B), and biological markers in cerebrospinal fluid (determination of AB42 peptide, Tau protein, and its phosphorylated form P-Tau 181) [13].

New criteria have been proposed for diagnosing AD in vivo, including the 2014 IWG-2 "International Work Group Criteria for the Diagnosis of Alzheimer's Disease". These criteria identify four possible diagnoses, as presented in Table 1 [14].

Table n°1: IWG-2 criteria for typical AD (A plus B at any stage)

A Specific clinical phenotype
• Presence of an early and significant episodic memory impairment (isolated or associated with other cognitive or behavioural changes that are suggestive of a mild cognitive impairment or of a dementia syndrome) that includes the following features:
◦ Gradual and progressive change in memory function reported by patient or informant over more than 6 months
◦ Objective evidence of an amnestic syndrome of the hippocampal type,* based on significantly impaired performance on an episodic memory test with established specificity for AD, such as cued recall with control of encoding test
B In-vivo evidence of Alzheimer's pathology (one of the following)
• Decreased $A\beta_{1-42}$ together with increased T-tau or P-tau in CSF
• Increased tracer retention on amyloid PET
• AD autosomal dominant mutation present (in *PSEN1*, *PSEN2*, or *APP*)

AD=Alzheimer's disease. *Hippocampal amnestic syndrome might be difficult to identify in the moderately severe to severe dementia stages of the disease, in which in-vivo evidence of Alzheimer's pathology might be sufficient in the presence of a well characterised dementia syndrome. †Additional investigations, such as blood tests and brain MRI, are needed to exclude other causes of cognitive disorders or dementia, or concomitant pathologies (vascular lesions).

IV. Risk Factors For Dementia And Alzheimer's Disease

The etiology of neurodegenerative dementias is still poorly understood, but it is now accepted that they are complex and multifactorial [15].

Age is the primary risk factor for dementia. The prevalence of dementia doubles every five years from the age of 65 onwards [16].

Female gender [16] and apolipoprotein E (APOE4) genotype [17] are also important risk factors, particularly for AD.

Vascular factors (hypertension, diabetes, obesity), lifestyle factors (smoking, excessive alcohol consumption, sedentary lifestyle), and depression are also important risk factors [18]; but, unlike the former, these factors are modifiable. It has been estimated that a third of AD cases are attributable to these factors [19], and therefore potentially preventable.

A number of other factors that can be grouped under the heading of "psychosocial factors" (poor social network, stress, etc.) are also thought to play a role in the development of dementia [18, 20]. It would seem that it is the accumulation of these factors throughout life that contributes to the development of dementia syndrome [18, 21].

V. Epidemiology Of Dementia And Alzheimer's Disease Worldwide And In Algeria

In 2019, the World Alzheimer Report estimated that there were 55.2 million people with dementia worldwide and predicted that this number would increase to 78 million in 2030 and 139 million in 2050 [1].

The prevalence of age-related dementias and Alzheimer's disease (AD) is therefore on the rise. The latest estimates put the number of people with dementia worldwide at 46.8 million in 2015 [1]. This figure is set to almost double every 20 years, reaching 74.7 million in 2030 and 131.5 million in 2050. These new estimates are 12-13% higher than those made for the 2009 World Alzheimer's Report. Most of this increase is attributed to low- and middle-income countries; 58% of all people with dementia currently live in countries classified by the World Bank as low- or middle-income. This proportion is expected to rise to 63% in 2030 and 68% in 2050 [1].

East Asia is the region with the highest number of people living with dementia (9.77 million), closely followed by Western Europe (7.45 million), South Asia (5.13 million), and North America (4.78 million).

The nine countries with the highest number of people with dementia in 2015 were: China (9.5 million), the USA (4.2 million), India (4.1 million), Japan (3.1 million), Brazil (1.6 million), Germany (1.6 million), Russia (1.3 million), Italy (1.2 million), Indonesia (1.2 million), and France (1.2 million).

In the 2015 World Alzheimer Report, the global crude prevalence rate of dementia in subjects aged 60 and over was estimated at 5.2%.

VI. Current Situation In Algeria:

An nalysis of the changing age structure of the Algerian population shows that our country is no exception to the universal demographic phenomenon of aging.

The proportion of elderly people in Algeria is rising steadily, reflecting a longer life expectancy. The proportion of the population aged 60 and over rose from 6.7% in 1966 to 8.9% in 2016. Life expectancy at birth is now around 78 years (77 for men and 78 for women) [22]. Furthermore, demographic projections suggest that the aging of the Algerian population will continue in the years and decades to come. These projections show that the proportion of the population aged 60 or over will double over the next 20 years.

In addition, the aging of the Algerian population is accompanied by an increase in the incidence of "age-dependent" chronic pathologies. These include dementia, which is likely to be a major public health issue.

A major epidemiological study carried out from 2012 to 2014 , by the team at the neurology department of CHU Mustapha, Algiers Centre, under the direction of Pr Meriem TAZIR, estimated the overall prevalence of dementia in the daïra of Sidi M'Hamed, Algiers Centre, among subjects aged 60 and over at 4.93%, and that of Alzheimer's disease at 3.54%. This study estimated the number of people suffering from dementia in Algeria at 151,346 patients, including 108,772 cases of Alzheimer's disease.

Based on the Delphi consensus [23], the same team estimated the number of demented subjects in 2016 at 189,182 patients, including 135,849 cases of Alzheimer's disease. Among the modifiable risk factors for dementia most frequently found in this study were: low cultural level, lack of occupation, isolation, high blood pressure, diabetes, heart disease, stroke and head trauma.

These figures are worrying and should prompt the Algerian authorities to implement a national public health plan to combat this disease. The aim of this plan is to facilitate the diagnosis and treatment of dementia and Alzheimer's disease, and to improve the quality of life of patients and their families.

Since 2004, memory consultations have been set up in various university hospital centers across the country, enabling early diagnosis of dementia and specific "drug and cognitive" treatment. A number of independent daycare centers have also been set up in Algiers, offering patients activities to stimulate their cognitive functions and providing family caregivers with a respite solution to relieve them of their onerous daily tasks of caring for their loved ones.

A local Algiers-Alzheimer Association was set up in 2005, at rue des frères BELLILI in the Casbah, to raise awareness, inform and assist relatives of Alzheimer's sufferers, as a complement to medical care. Knowledge of the risk factors for dementia, which are the most common in our population, underlines the importance of proposing preventive measures that will enable us to reduce the incidence of dementia in Algeria in the future. This is a priority for public health.