Risk Factors for Dementia and Impaired Cognitive Status in Thai Elderly†

VORAPUN SENANARONG, M.D., M.R.C.P. (UK.)*,
KAMONTIP HARNPHADUNGKIT, M.D.**,
SUTHIPOL UDOMPUNTHURAK, M.Sc****,
NIPHON POUNGVARIN, M.D., F.R.C.P. (London)*
PIYANUCH JAMJUMRUS, B.Sc.*,
SATHIT VANNASAENG, M.D.***,
NARAPORN PRAYOONWIWAT, M.D.*,

Abstract

Objective : To examine the association of physical and biochemical risk factors for dementia and cognitive status in an urban population based Thai elderly.

Material and Method : This study was part of an integrated health research project from 1997 to 1999. Subjects were 550 elders who lived in a community within 10 km from Siriraj Hospital, Bangkok, Thailand. They were 55 years and older. Thai mental state examination (TMSE) was applied to all subjects as the screening test for dementia. Those who scored less than or equal to 24 out of 30 were categorised as having cognitive impairment or suspected of having dementia, and they were then examined in detail for the diagnosis of dementia using the DSM IV criteria. Blood pressure and body weight were recorded. Blood was drawn for biochemical and haematological analysis including the serology for syphilis and thyroid function test as the basic screening investigation for dementia. Descriptive data, expressed as the mean, standard deviation, Pearson Chi square and ANOVA tests were analysed with SPSS 9.0 in the study.

Results : Of 550 subjects, 261 (47.45%) were classified as the normal subjects group, 49 (8.91%) as the cognitively impaired group, and 240 (43.82%) as the dementia group. 377 subjects (68.55%) were female and the distribution of females in each subgroup ranged from 63.3 - 75.5 per cent. The mean age in the normal group was 67.47 $\pm$ 6.05 years, the cognitively impaired group was 70.14 years and the dementia group was 69.63 $\pm$ 9.21 years. Systolic blood pressure (BP), diastolic BP, serum cholesterol, SGOT, GGT, serum albumin, haemoglobin, MCHC, neutrophil counts and weight were statistically significant factors that were associated with cognitive status. Both systolic and diastolic BP were high in the higher cognitive status group. Serum albumin, serum cholesterol levels and body weight were also higher in the high cognitive status group.

Conclusion : This study demonstrated an association between nutritional status and cognitive status in Thai elderly. Poorer nutritional factor in lower cognitive function individuals might explain a lower of both systolic and diastolic BP in the dementia subjects compared to the healthy subjects.

Key word : Risk Factors, Dementia, Cognitive Impairement, Thai Elderly

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* Division of Neurology, Department of Medicine,
** Department of Rehabilitation Medicine,
*** Division of Endocrinology, Department of Medicine,
**** Division of Clinical Epidemiology, Department of Research and Development, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.
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There are two forms of dementia, reversible and non-reversible. Two related factors are important: the prevalence of reversible dementia and the outcome of treatment of reversible dementia. Clarfield published a monograph stating that partial recovery was seen in 8 per cent and full recovery in 3 per cent of patients[1]. Treatment of reversible dementia has the best results in its most frequent causes: depression and drug intoxication[2]. Blood tests looking for etiology of reversible dementia in every patient with dementia are still recommended.

Another traditional assumption is that there are two forms of dementia Alzheimer's disease (AD) and vascular dementia (VaD). Recent epidemiological evidence shows that vascular risk factors may possibly be important in the etiology of dementia in general and of both VaD and AD[3-5]. Blood pressure (BP) has been an interesting focus on cognitive function and is viewed as a potential reversible risk factor for dementia. Elevated BP and hypertension are known to be associated with the presence and with amount of white matter hyperintensities (WMHIs)[6-8] and cerebral atrophy[9]. Evidence suggests that larger volumes of WMHI are associated with lower levels of cognitive function[10].

Our study aimed to examine the relationship between blood pressure (BP), physical, haematological and biochemical risk factors and cognitive status in Thai elderly.

MATERIAL AND METHOD

This study was part of the Integrated Health Research Project for Thai Elderly at the Faculty of Medicine Siriraj Hospital conducted from 1997 to 1999. A door to door survey and record of the elderly dwelling in the area within 10 km around Siriraj Hospital, Bangkok, was performed. Names of these elders were recorded as participants in the study. Their ages were fifty-five years and older. Of these 550 subjects were recruited for our case-control study. We categorised the elders into the dementia group, the cognitive impairment group and the normal group. Thai Mental State Examination (TMSE)[11] was applied as a screening cognitive test for all subjects. Those whose score being less than or equal to 24 out of 30 but did not meet the criteria for diagnosis of dementia, were defined as cognitively impaired. Dementia was diagnosed according to the DSM IV criteria[12].

Arterial blood pressure was measured with a mercury sphygmomanometer with subjects

sitting and resting for an hour before the recording. Two readings were done and the lower reading was recorded. Systolic and diastolic blood pressure were defined as Korotkoft phases 1 and 5 respectively.

All subjects had six hours of overnight fasting and blood was drawn the next morning for haematological and biochemical analyses, serology for syphilis and the thyroid function tests. Body weight was recorded in the morning.

All analyses were conducted with SPSS 9.0 statistical software. Descriptive analyses, ANOVA, Bonferroni post hoc multiple comparisons and Pearson Chi square test were used in this study.

RESULTS

There were 261 elders who were cognitively normal and mobile. Two hundred and forty subjects met DSM IV criteria for the diagnosis of dementia. Etiologies of dementia were not explored in these subjects. Forty-nine elders were recruited as a cognitively impaired group (Table 1). The majority in these three groups of elders were female, and they were aged less than 80 years.

Biochemically, there was statistically significant difference among the three groups in serum cholesterol, liver enzymes and serum albumin levels. Although the mean concentration of liver enzymes in these three groups were different, it was not clinically significant. Other parameters of the liver function test were normal. The higher the levels of serum cholesterol, and serum albumin, the higher the cognitive status of the elderly. From our observation, we found a higher body weight in the group of higher cognitive status group. These biochemical parameter differences could be explained by a nutritional status factor. However, we did not explore other confounders such as history of antihypertensive medication, chronic illnesses, educational levels and depression.

There were some haematological parameters that showed significant difference among the three groups. However, these figures were not clinically significant.

DISCUSSION

Four to ten per cent of the Thai elderly had an abnormal thyroid function test, but none had clinical hypothyroidism or hyperthyroidism. An abnormal thyroid status when treated is a reversible condition. This high prevalence confirms the added value of diagnostic tests for reversible dementia. A positive serology for syphilis was found in upto fourteen per cent in the elderly which suggested that a thorough investigation for potential treatable causes for dementia are necessary, including routine screening tests for thyroid function and syphilitic infection in the Thai subjects with dementia.

Weight loss has been shown to be associated with the severity and progression of Alzheimer's disease (AD)[13] and may occur before a diagnosis of AD[14]. We confirm that in our cross-sectional study weight loss occurred before the diagnosis of dementia. However, other acute or chronic illnesses may contribute to weight loss. We did not explore these confounding factors. In our results, acute phase responses in blood tests did not show a clinically signifi-

Table 1. Subject characteristics.

	Dementia (n=240)	Cognitive impairment (n=49)	Normal subjects (n=261)
Sex : Male n (%)	81 (33.8)	12 (24.5)	77 (29.5)
Female n (%)	159 (63.2)	37 (75.5)	184 (70.5)
Age : ≤ 69yrs n (%)	116 (48.3)	25 (51)	170 (65.6)
70-79yrs n (%)	89 (37.1)	18 (36.7)	78 (30.1)
80yrs n (%)	35 (14.6)	6 (12.2)	11 (4.2)
mean±SD (yrs)	69.63±9.21	70.14±7.19	67.47±6.05
range (yrs)	57-96	60-87	55-85
TMSE (mean±SD)	17.89±7.36	20.92±2.87	26.7±1.87

Table 2. Association of physical factors and blood results with cognitive status in Thai elderly (mean±SD).

	Dementia	Cognitive impairment	Normal subjects	p value
Systolic BP (mmHg)	134±22	139±25	141±24	0.009**
Diastolic BP (mmHg)	81±11	83±13	86±13	0.001**
Fasting blood glucose (mg/dL)	119±56	114±56	119±62	0.884
BUN (mg/dL)	16.5±8.8	16.5±8.8	16.6±8.7	0.992
Creatinine (mg/dL)	1.14±0.71	1.06±0.27	1.03±0.22	0.137
Cholesterol (mg/dL)	231±53	251±51	250±51	0.001**
Triglyceride (mg/dL)	158±116	178±80	167±106	0.461
HDL (mg/dL)	53±18	53±15	53±15	0.997
LDL (mg/dL)	163±41	161±49	163±44	0.959
SGOT (unit/L)	28±19	36±51	27±11	0.024*
GGT (unit/L)	22.8±16	48.6±63.4	39.6±42	0.040*
Alkaline phosphatase (unit/L)	91±35	95±29	92±34	0.881
Total protein (g/dL)	7.9±0.6	8.1±0.5	8.0±0.7	0.418
Albumin (g/dL)	4.3±0.6	5.1±0.4	4.9±0.7	<0.001***
Total bilirubin (mg/dL)	0.67±0.75	0.66±0.54	0.59±0.23	0.307
Serum T_4 (microgm/dL)	9.5±10.7	8.2±1.8	8.2±2.1	0.152
TSH (micro unit/mL)	2.2±6.8	1.7±3.5	1.8±2.5	0.668
Hemoglobin (g/dL)	12.9±1.8	13.2±1.7	13.4±1.6	0.004**
Hematocrit (%)	39.2±5.0	40.5±4.7	41.1±5.1	0.001**
WBC ($x10^3\mu L$)	7.3±7.4	7.5±2.2	6.8±1.7	0.494
MCV (fL)	87.2±9.8	89.8±8.9	89.0±7.7	0.060
MCHC (g/dL)	32.8±1.5	32.5±1.5	32.2±1.9	0.004**
Platelet count ($x10^3/\mu L$)	270±106	294±83	260.5±67.2	0.034*
Neutrophil (%)	59.0±12.6	53.5±9.2	53.3±28.0	0.020*
Eosinophil (%)	3.7±4.5	3.3±2.5	4.1±3.7	0.355
Weight (kgms)	53.59±10.94	54.79±10.48	57.77±11.33	0.001**

* < 0.05, ** < 0.01, *** < 0.001

cant change. Only those which were nutritionally related such as serum cholesterol, serum triglyceride and serum albumin levels showed a significant change in the relation to weight change. In the population studies of elderly, weight loss was shown to be predictive of the mortality(15, 16). In AD, weight loss of ≥ 5 per cent in any patient was a significant predictor of mortality (17). Some population-based data suggest that a lower mortality rate occurs among people who gain small to moderate amounts of body weight in comparison to people who lose weight(18). Our study suggests that more attention to nutrition should be beneficial for the elderly with cognitive impairment or with dementia.

Hyperglycemia is a known vascular risk factor for dementia. It compounds ischaemic burden of the brain by increasing anaerobic metabolism and lactic acidosis overproduction (19). It is associated with insulin resistance(20) and decreased cholinergic transport across the blood-brain barrier(21). Nevertheless, in this sample set of data, we did not find any positive relationship of hyperglycemia with dementia. This may be due to heterogeneity of our dementia group which had not been fully investigated.

We demonstrated that blood pressure had a tendency to decrease as the cognitive function declined. Blood pressure has statistically significant association with cognitive function. We did not have information on anti-hypertensive medication in these elders. However, in a previous report from the Kungsholmen Project(22), they conducted a cross-sectional community-based Swedish cohort of 1,736 people aged between 75-101 years, and then retested them after an average follow-up period of 40.5 months. They found no significant relationship between low or high blood pressure and the risk of developing cognitive impairment among persons taking or not taking antihypertensive medication. At baseline study, they found that both systolic and diastolic blood pressures were positively and significantly related to the mini mental state

Table 3. Percentages of abnormalities in physical factors and blood results in association with cognitive status in Thai elders.

	Dementia	Cognitive Impairment	Normal Subjects	p-value
Systolic BP ≥140 mmHg	46.0	49.0	53.8	0.252
Diastolic BP ≥90 mmHg	36.3	53.1	53.8	0.001*
Fasting blood glucose ≥126 mg/dL	25.8	16.3	22.5	0.372
BUN >20 mg/dL	14.2	20.4	14.3	0.517
Creatinine >1.5 mg/dL	8.5	-	4.2	0.031*
Cholesterol >200 mg/dL	77.0	83.7	88.0	0.011*
Triglyceride >200 mg/dL	19.8	32.7	24.4	0.158
HDL <35 mg/dL	10.8	8.2	5.8	0.198
LDL >160 mg/dL	40.9	43.9	52.2	0.406
SGOT >40 unit/L	13.2	16.3	10.4	0.427
GGT >50 unit/L	6.5	28.6	17.9	0.041*
Alkaline phosphatase >117 unit/L	12.7	10.2	12.0	0.899
Total protein <6.6 g/dL	3.2	-	1.2	0.430
Albumin <3.5 or >5.5 g/dL	9.3	12.2	16.6	0.102
Total bilirubin >1.2 mg/dL	5.8	6.1	1.9	0.086
Serum T_4 <4.5 μg/dL	8.6	4.1	5.8	0.395
TSH >4 microunit/mL	10.6	10.2	10.9	0.988
VDRL-reactive	2.8	4.1	2.7	0.864
TPHA-reactive	7.2	14.3	10.4	0.272
Hemoglobin <12 or >18 g/dL	27.9	26.5	13.1	<0.001*
Hematocrit <37 or >52 g/dL	34.8	24.5	15.1	<0.001*
WBC <4 or >11x10^3/μL	11.6	10.2	3.9	0.006
MCV >100 fL	3.8	10.2	3.5	0.097
MCHC <33 g/dL	52.2	63.3	69.1	0.003*
Platelet count <440x10^3/μL	5.1	4.1	1.2	0.047
Eosinophil >7%	15.2	8.2	13.5	0.447

examination (MMSE) score. So, we conclude that the actual blood pressure per se has an effect on cognition regardless of antihypertensive medication. Prince MJ et al[23] also found that antihypertensive medication seems to have little or no effect on the association or cognitive impairment. They concluded that it favoured the importance of underlying pathology rather than a direct effect of blood pressure itself on cognitive decline. In the Goteborg Study[24], a longitudinal population based examination of a cohort of 382 normal subjects was conducted and found that eighteen participants who developed dementia between the age 79 and 85 had significantly higher systolic blood pressure at 70 and higher diastolic pressure at 70 and 75 than those who did not develop dementia. The association between high blood pressure and cognitive declination remains controversial. In the Honolulu-Asia Aging Study[26] and the Framingham Study,[26] they showed no association between high blood pressure and cognition in their cross sectional analysis but there was strong association in the longitudinal analysis. Our study demonstrated there was a significantly lower level of blood pressure in the group with cognitive impairment. We also demonstrated poorer nutritional status namely body weight, cholesterol and albumin levels, in the cognitive decline groups. Therefore, this poorer nutritional status may be related to lower blood pressure or may even be a cause of lower blood pressure.

In conclusion, we demonstrated an association of poor nutritional status and low blood pressure levels with the cognitive impaired status in Thai elderly. Careful nutritional evaluation in persons with a cognitive problem is required. A Public Health policy should emphasise primary and secondary prevention concerning poor nutrition status in older adults in Thailand.

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ความสัมพันธ์ของปัจจัยเสี่ยงทางกายภาพและชีวเคมีต่อภาวะสมองเสื่อมในผู้สูงอายุไทย†

วรพรรณ เสนาณรงค์, พ.บ., ปิยนุช แจ่มจำรัส, พย.บ.*,*
*กมลทิพย์ หาญผดุงกิจ, พ.บ.**, สาธิต วรรณแสง, พ.บ.***,*
*สุทธิพล อุดมพันธุรัก, วท.ม.****, นาราพร ประยูรวิวัฒน์, พ.บ.*, นิพนธ์ พวงวรินทร์, พ.บ.**

วัตถุประสงค์ : ผู้วิจัยได้ศึกษาหาความสัมพันธ์ของปัจจัยทางกายภาพและปัจจัยทางชีวภาพ ที่จะเป็นปัจจัยเสี่ยงต่อการเกิดภาวะสมองเสื่อมและต่อสมรรถภาพการทำงานของสมองในผู้สูงอายุไทยที่อยู่อาศัยในชุมชนเมือง

วิธีการ : การศึกษานี้เป็นส่วนหนึ่งของ การศึกษาและวิจัยปัญหาสุขภาพผู้สูงอายุไทย (วสส) ซึ่งดำเนินการศึกษาโดยคณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล ระหว่างปี พ.ศ.2540–2542 ที่ศึกษาประชากรผู้สูงอายุที่อาศัยอยู่ในชุมชนภายในอาณาเขต 10 กิโลเมตรรอบวิทยาเขตศิริราช ประชากรที่ศึกษานี้มีจำนวน 550 ราย และมีอายุ 55 ปีขึ้นไป ได้ใช้แบบทดสอบสมรรถภาพสมองไทย (Thai mental state examination, TMSE) เพื่อเป็นการตรวจสอบคัดกรองภาวะสมองเสื่อมในผู้สูงอายุทุกคน ผู้สูงอายุที่ได้คะแนน น้อยกว่าหรือเท่ากับ 24 จาก คะแนนเต็ม 30 คะแนน ถือว่ามีการทำงานของสมองบกพร่อง (cognitive impairment) และจะถูกนำมาตรวจและทดสอบโดยละเอียดเพื่อวินิจฉัยว่ามีภาวะสมองเสื่อมหรือไม่โดยอาศัยเกณฑ์ของ DSM IV คณะผู้วิจัยได้จดบันทึกน้ำหนักและความดันโลหิตของผู้สูงอายุทุกราย พร้อมเจาะเลือดของผู้สูงอายุเพื่อนำมาวิเคราะห์ทางโลหิตวิทยา ชีววิทยาและทดสอบด้านการติดเชื้อซิฟิลิส และการทำงานของต่อมธัยรอยด์ โดยที่ถือเป็นการสืบค้นหาสาเหตุของภาวะสมองเสื่อมที่ต้องตรวจทุกราย การวิเคราะห์ข้อมูลทางสถิติทั้งหมดใช้โปรแกรม SPSS 9.0

ผลการวิจัย : ประชากรผู้สูงอายุที่ศึกษา 550 ราย จำแนกเป็นกลุ่มคนปกติ 261 ราย (ร้อยละ 47.45) กลุ่มผู้ที่มีการทำงานของสมองบกพร่อง 49 ราย (ร้อยละ 8.91) และในกลุ่มผู้ป่วยสมองเสื่อม 240 ราย (ร้อยละ 43.82) ประชากร 377 ราย (ร้อยละ 68.55) เป็นผู้หญิงและการกระจายของเพศหญิงในแต่ละกลุ่มศึกษาอยู่ในอัตราร้อยละ 63.3 ถึง 75.5 ในแต่ละกลุ่มที่ศึกษา อายุโดยเฉลี่ย คือ 67.47±6.05 ปีในกลุ่มปกติ, 70.14+7.19 ปีในกลุ่มที่มีการทำงานของสมองบกพร่อง และ 69.63+9.21 ปีในกลุ่มสมองเสื่อม ปัจจัยที่มีความสัมพันธ์กับสมรรถภาพการทำงานของสมอง (cognitive status) ได้แก่ ความดันโลหิตสิสโตลี และ ไดแอสโตลี, ระดับไขมันในเลือดที่มากกว่าหรือเท่ากับ 150 มิลลิกรัมต่อเดซิลิตร, ระดับ SGOTและ GGT, ระดับแอลบูมินในเลือด, ฮีโมโกลบิน, MCHC, จำนวน นิวโตรฟิล และน้ำหนักของผู้สูงอายุ ความดันโลหิตทั้ง สิสโตลี และ ไดแอสโตลี จะมีค่าสูงในกลุ่มผู้ที่มีสมรรถภาพการทำงานของสมองที่ดี ระดับแอลบูมิน, โฆเลสเตอรอลในเลือดและน้ำหนักของผู้สูงอายุ จะมีค่าสูงกว่าผู้สูงอายุที่มีสมรรถภาพการทำงานของสมองที่ดีเช่นกัน

สรุป : การศึกษาวิจัยครั้งนี้ พบว่ามีความสัมพันธ์กันที่ชัดเจนของภาวะโภชนาการ และสมรรถภาพการทำงานของสมอง การที่มีภาวะโภชนาการของร่างกายที่ไม่ดีในผู้ที่มีการทำงานของสมองบกพร่องนั้น อาจอธิบายถึงสาเหตุของการที่มีความดันโลหิตต่ำ และทำให้มีการทำงานของสมองบกพร่องเกิดขึ้นได้

คำสำคัญ : ปัจจัยเสี่ยง, ภาวะสมองเสื่อม, สมรรถภาพของสมอง, ผู้สูงอายุไทย

วรพรรณ เสนาณรงค์, ปิยนุช แจ่มจำรัส, กมลทิพย์ หาญผดุงกิจ, และคณะ
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* สาขาวิชาประสาทวิทยา, ภาควิชาอายุรศาสตร์,
** สาขาวิชาเวชศาสตร์ฟื้นฟู,
*** สาขาวิชาต่อมไร้ท่อ, ภาควิชาอายุรศาสตร์,
**** หน่วยระบาดวิทยา, สถานส่งเสริมการวิจัย,คณะแพทยศาสตร์ศิริราชพยาบาล, มหาวิทยาลัยมหิดล, กรุงเทพฯ 10700
† การศึกษานี้ได้รับเงินสนับสนุนจากสภาวิจัยแห่งชาติ เงินทุนวิจัยปีงบประมาณปี พ.ศ.2540–2542