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INTRODUCTION

Alzheimer's disease (AD) is becoming a greater burden on the global aging population. The incubation period of AD can be as long as 20-30 years. Identifying high-risk groups during the incubation period, before the onset of clinical symptoms, has remained an unsolved problem. β-amyloid precursor protein (AβPP) is a protein that protects neural synapses and regulates neuronal excitability, synaptic activity, signal transmission and plasticity. Its secretion increases when neurons are stressed or damaged. Increased AβPP is found not only in the cerebrospinal fluid (CSF) and blood of AD patients (especially those who do not carry APOE ε4) , but also in other types of neurodegenerative diseases such as motor neuron disease. Therefore, elevated AβPP is a biomarker of impaired brain health, not just AD. Persistently elevated AβPP may indicate persistent brain problems and could potentially lead to AD or other types of dementia.

Qankorey Biotechnology has launched the world’s first urine β-amyloid protein detection kit (Zhu et al, J Alzhei Dis, 2025) . It uses a unique antibody-antigen-polymer high-sensitivity sandwich method for detection. Published data shows that it can distinguish mild cognitive impairment (MCI) patients who have not yet developed Aβ plaques. Moreover, it performed well in the screening of 11 cities in Jiangsu Province organized by the Jiangsu Provincial Health Commission in 2023 [20]. Since there is strong demand for a simple and inexpensive biomarker-based tool that can be used for primary community screening, it is necessary to determine whether this product meets those needs. Meanwhile, the product can also be used for self-testing at home, which can supplement the shortcomings of community screening and protect personal privacy [21].

Besides the lack of suitable screening methods, another challenge in screening for cognitive decline risk in the elderly is the impact of comorbidities and medications on screening results. In reality, most older adults have various common illnesses, such as high blood sugar, high blood pressure, high cholesterol, and memory loss. It is unknown what confounding impacts, if any, these common illnesses and their medications have on cognitive decline or improvement. Currently, there are no good methods to measure and assess these factors. In this study, we collected relevant information to try and determine any impact of those factors

METHODS

Multicenter validation: Yuquan Hospital of Tsinghua University, Beijing Tiantan Hospital and Beijing Friendship Hospital of Capital Medical University, Zibo No. 148 Hospital in Shandong Province, and the Third People's Hospital of Yunnan Province participated in this work. Participants were over 55 years of age, regardless of gender. The healthy control group consisted of participants without any known age-related diseases and who did not regularly take medications. The mild cognitive impairment (MCI) and Alzheimer's disease (AD) groups consisted of clinically diagnosed outpatients or inpatients with MCI or AD, the vast majority of whom were undergoing treatment. The non-AD disease group consisted of elderly individuals with diseases (excluding MCI or AD) but normal cognition, the vast majority of whom were continuously taking medications. The Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), and the Qankorey® Urine β-Amyloid Protein Detection Kit (also known as “One-Step Dementia Risk Test Kit”) developed by Qankorey Biotechnology, Changsha, China, were used for testing.

Community Screening: In response to the national call to promote the prevention and control of AD, the Yuhua District People's Government and the Yuhua Economic Development Zone Management Committee of Changsha City, Hunan Province, actively coordinated and organized the screening program. The Yuhua District Health and Wellness Bureau and the Yuhua District Center for Disease Control and Prevention provided on-site coordination, meticulous organization, and full mobilization. From March to December 2024, free early screening and prevention services for dementia were conducted for individuals aged 50 and above in 14 community health service centers/hospitals within the Yuhua district. A total of 51,187 people were tested.

Statistical methods: We used the chi-square test (χ² test) and Fisher's exact test to detect differences between groups. The Kappa test was used to evaluate the clinical diagnostic value of the test strips: 0.81–1 was highly consistent, 0.61–0.8 was good consistent, 0.41–0.6 was moderately consistent, 0.21–0.4 was reasonably consistent, and < 0.2 was poor.

RESULTS

Table 1: Summary Data of Multicenter Clinical Trials

	HC	Non-AD	MCI	AD	MCI+AD
Number (male/female)	266 (107/159)	465 (237/228)	24 (12/12)	143 (50/93)	167 (62/105)
Age (χ ² ± s)	65.4±10.3	67.0±8.4	70.7±8.2	70.7±9.8	70.7±9.6
Weak positive	8	41	16	61	77
Positive	12	16	3	41	44
Negative	246	409	5	41	46
% Positive	7.5%	12.2%	79.2%	71.3%	72.5%
P value	-	0.0286	2.60×10 ⁻¹³	1.01×10 ⁻⁴¹	1.14×10 ⁻⁴⁶

Comparing HC and MCI/AD groups:
positive concordance rate (sensitivity): 72.5%;
negative concordance rate (specificity): 92.5%;
Kappa (κ) value 0.669
Comparing HC and MCI groups:
sensitivity was 79.2%, specificity was 92.5%, Kappa (κ) value was 0.558

Table 2: Performance of urine Aβ test strips in different cognitive populations

	MMSE score			
	27-30	23-26	10-22	<10
Test strip positive	69	18	67	43
Test strip negative	515	47	115	15
Positive rate	11.8%	27.7%	36.8%	74.1%
p-value	0.0009	0.1190	5.76×10 ⁻⁷	
	MoCA score			
	>25	18-25	10-17	<10
Test strip positive	35	50	25	34
Test strip negative	376	194	52	17
Positive rate	8.5%	20.5%	32.5%	66.7%
p-value	1.23×10 ⁻⁵	0.0248	0.0001	

Table 3: Urine Aβ test strips in ApoE Performance in ε4 and non-ε4 populations

	Cognitively Normal		MCI+AD		Everyone	
	ε4 ⁺	ε4 ⁻	ε4 ⁺	ε4 ⁻	ε4 ⁺	ε4 ⁻
Test strip positive	0	6	25	26	25	32
Test strip negative	9	26	19	13	28	39
Positive rate	0	18.7%	56.8%	66.7%	47.2%	45.1%
p-value	0.2015		0.2441		0.4798	

Table 5: Performance of urine Aβ test strips in populations taking different medications

Treatment medication	Strip Results			P
	Pos	Neg	Pos rate	
Non-AD treatment drugs	17	359	4.5%	4.53 × 10 ⁻⁵
Antithrombotic	4	96	4.0%	0.0081
Lipid-lowering	9	102	8.1%	0.1433
Antihypertensive	11	140	7.3%	0.0581
Hypoglycemic agents	2	53	3.6%	0.0358
Brain-improving	2	31	6.1%	0.2249
Cardiovascular	0	41	0	0.0060
Dizziness and tinnitus	0	36	0	0.0110
AD treatment drugs	72	38	65.5%	0.1303
Memantine hydrochloride	25	18	58.1%	0.0532
GV-971	65	34	65.7%	0.1514
Donepezil hydrochloride	41	12	77.4%	0.3031

CONCLUSION

The test strip shows high feasibility and reasonable accuracy as a screening tool for cognitive decline in a large population. Our findings confirm the diagnostic value of urinary β-amyloid protein detection in MCI and AD-related dementia. Furthermore, this kit can be used in practical clinical applications to assess the risk of cognitive decline of various comorbidities and treatment efficacy across various diseases.

Table 4-1: Performance of urine Aβ test strips in all populations with or without different comorbidities

Comorbidities	With comorbidities			No comorbidities			P
	Pos	Neg	Positive rate	Pos	Neg	Positive rate	
Hypertension	106	302	26.0 %	92	399	18.7 %	0.0058
Hyperglycemia	37	155	19.3 %	161	546	22.8 %	0.1739
Hyperlipidemia	73	96	43.2 %	125	605	17.1 %	3.25×10 ⁻¹²
History of Stroke	22	32	40.7 %	176	669	20.8 %	0.0011
Heart disease	11	56	16.4 %	187	645	22.5 %	0.1590
Parkinson's disease	3	8	27.3 %	195	693	22.0 %	0.4499
Sleep disorders	6	20	23.1 %	192	681	22.0 %	0.5260
Frequent dizziness	38	343	10.0 %	159	358	30.8 %	1.26×10 ⁻¹⁴
Memory loss	102	112	47.7 %	96	589	14.0 %	9.67×10 ⁻²³
Brain diseases	5	13	27.8 %	193	688	21.9 %	0.3617
Limb weakness	22	94	19.0 %	176	607	22.5 %	0.2346
Inflammation	2	15	11.8 %	196	686	22.2 %	0.2399
Anxiety	6	6	50.0 %	192	695	21.6 %	0.0297

Table 4-2: Performance of urine Aβ test kit in cognitively normal participants with or without different comorbidity

Comorbidities	With comorbidities			No comorbidities			P
	Pos	Neg	Positive rate	Pos	Neg	Positive rate	
Hypertension	46	277	14.2	31	378	7.6	0.0027
Hyperglycemia	19	148	11.4	58	507	10.3	0.3871
Hyperlipidemia	23	77	23.0	54	578	8.5	6.34×10 ⁻⁵
History of Stroke	16	32	33.3	61	623	8.9	7.39×10 ⁻⁶
Heart disease	7	55	11.3	70	600	10.4	0.4845
Parkinson's disease	2	7	22.2	75	648	10.4	0.2427
Sleep disorders	6	20	23.1	71	735	10.1	0.0461
Frequent dizziness	27	343	7.3	50	312	13.8	0.0028
Memory loss	102	112	13.9	96	589	10.1	0.1942
Brain diseases	5	13	18.8	193	688	10.3	0.2319
Limb weakness	22	94	8.8	176	607	10.8	0.3447
Inflammation	2	15	11.8	196	686	10.5	0.5493
Anxiety	6	6	44.4	192	695	10.1	0.0095

Table 6: Results of Community-wide Screening in Yuhua District

Age group	Number of people (male/female)	Number of negative	Number of positive	Positive rate (%)
< 46	334 (188/146)	313 (176/137)	21 (12/9)	6.3 (6.4/6.2)
46-59	3711 (1367/2344)	3421 (1274/2147)	290 (93/197)	7.8 (6.8/8.4)
60-69	20198 (8535/11663)	18387 (7847/10540)	1811 (688/1123)	9.0 (8.1 / 9.6)
70-79	21440 (9621/11819)	19351 (8801/10550)	2089 (820/1269)	9.7 (8.5/10.7)
80-89	5095 (2268/2827)	4469 (2012/2457)	626 (256/370)	12.3 (11.3/13.1)
> 89	409 (180/229)	346 (152/194)	63 (28/35)	15.4 (15.6/15.3)
Total	51187(22159/29028)	46287 (20262/26025)	4900 (1897/3003)	9.6 (8.6/10.4)

This work has been published in 中国阿尔茨海默病及相关病杂志 (Chinese Alzheimer’s Disease and Related Disorders, 9:150, 2026), the English version can be found at MedRxiv (<https://doi.org/10.64898/2026.05.06.26348372>).