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RESEARCH ARTICLE

THE LINK OF PHYSIOLOGICAL AND COGNITIVE DECLINE: EVIDENCE FROM AN AGING POPULATION IN URBAN INDIA

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Abstract

Background: Aging involves parallel deterioration across multiple physiological systems. Although cardiovascular, respiratory, cognitive, and psychological changes are well documented individually, their interdependence and combined impact on functional decline remain insufficiently explored, particularly in low- and middle-income country settings such as India.

Objectives: To examine the associations and potential mechanistic links among cardiovascular, respiratory, cognitive, and psychological functio ns in a community-dwelling urban elderly population in India.

Methods:A community-based cross-sectional study was conducted among 180 individuals aged ≥60 years residing in a Tier-2 city. Cardiovascular assessment included blood pressure and heart rate variability (HRV); respiratory function was evaluated using spirometry; cognitive performance was measured using the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA); and psychological distress was assessed using the GHQ-12 scale. Correlation analyses, hierarchical multiple linear regression, and k-means cluster analysis were employed to explore inter system relations hips.

Results: Higher systolic blood pressure and pulse pressure were inversely associated with cognitive scores,with the strongest correlation observed between pulse pressure and MoCA ($r = -0.30$, $p < 0.001$). Better pulmonary function, particularly higher FEV1, was positively correlated with cognitive performance (MMSE: $r = 0.25$, $p < 0.001$). Reduced HRV indices (SDNN, RMSSD) were significantly associated with greater psychological distress ($p < 0.001$). In multivariable regression,age, education, systolic blood pressure, FEV1 (% predicted), and GHQ-12 score independently predicted MoCA scores. Cluster analysis identified three distinct phenotypes: “Resilient Agers” (32%), “Vascular–CognitiveDecliners”(41%),and“Multisystem Compromised” (27%).

Conclusion: The findings demonstrate measurable interactions between cardiovascular, respiratory, cognitive, and psychological domains in older adults, with autonomic function and mental health acting as key intermediaries.

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These results support a multidomain understanding of aging and suggest that integrated interventions targeting vascular health, pulmonary function, and psychological well-being may help attenuate cognitive and functional decline in elderly populations.

Introduction:-

ging is accompanied by a progressive decline in physiological reserve across multiple organ systems, increasing susceptibility to chronic disease, disability, and loss of functional independence. Traditionally, age-related changes in cardiovascular, respiratory, or cognitive function have been examined largely in isolation, following a reductionist biomedical approach [1]. While such studies have contributed substantially to understanding individual disease processes, they do not adequately reflect the complex clinical reality of older adults, in whom impairments across several systems frequently coexist.Contemporary perspectives from systems biology and geroscience increasingly conceptualize aging as an emergent phenomenon arising from interconnected biological networks rather than isolated organ failure [2,3]. According to this framework, dysfunction in one physiological system may exacerbate decline in others through shared mechanisms such as inflammation, oxidative stress, vascular injury, and autonomic dysregulation. This interconnected decline provides a biological basis for multimorbidity, which has become a defining feature of aging populations worldwide, including in India [4].

Several mechanistic pathways have been proposed to explain cross-system interactions in aging. The vascular hypothesis emphasizes the role of arterial stiffness and endothelial dysfunction in compromising cerebral perfusion and damaging the brain's microvasculature, thereby contributing to cognitive impairment and dementia [5]. Complementing this, the hypoxia hypothesis suggests that age-related decline in respiratory function reduces oxygen delivery and promotes systemic inflammation, processes that are known to adversely affect neuronal integrity and cognitive performance [6]. A third pathway focuses on psychological stress and distress, which may activate neuroendocrine and inflammatory cascades that influence both cardiovascular regulation and brain health [7]. Although these mechanisms are supported by evidence from high-income countries, their relative contribution and interaction may differ in low- and middle-income settings due to variations in environmental exposures, lifestyle factors, and healthcare access.India is experiencing rapid demographic aging, with a growing proportion of older adults residing in Tier-2 cities. These urban environments often combine traditional cardiovascular and metabolic risk factors with additional stressors such as air pollution, changing family structures, and limited availability of geriatric-focused healthcare services [8]. High levels of ambient air pollution, in particular, may accelerate pulmonary decline while simultaneously promoting systemic inflammation, thereby strengthening links between respiratory, cardiovascular, and cognitive systems [9]. Despite this potentially heightened vulnerability, community-based research in India has largely focused on estimating the prevalence of individual chronic conditions, with few studies adopting an integrated, multisystem approach.

In this context, the present study was designed to examine aging as a multidimensional process by simultaneously assessing cardiovascular, respiratory, cognitive, and psychological domains in an urban elderly population. By analyzing correlations between physiological measures (including dynamic indices such as heart rate variability), pulmonary function, cognitive performance, and psychological distress, the study aimed to: (1) quantify cross-system associations, (2) identify independent predictors of cognitive function, and (3) explore distinct phenotypic patterns based on multisystem health profiles. Generating such context-specific evidence is essential for informing integrated strategies to preserve cognitive function and functional independence among India's rapidly growing elderly population.

Materials and Methods:-

Study Design and Setting:-

This was a community-based, cross-sectional, descriptive study conducted between January 2024 and June 2024 in a Tier-2 city. The city was purposively selected for its representative urban characteristics, including a mix of planned residential areas, slums, and transitional zones.

Study Population and Sampling:-

Sample Size:

The total sample size of 180 was determined using the formula for cross-sectional prevalence studies, assuming an anticipated morbidity prevalence of 65%, a 95% confidence level (Z = 1.96), and a relative precision of 10%.

Sampling:
The study population comprised community-dwelling individuals aged 60 years and older residing in defined urban administrative wards. A multistage random sampling approach was utilized to ensure representativeness:
First Stage: Two urban wards were selected at random—one representing a slum area and the other a non-slum residential zone—from the official municipal registry.
Second Stage: From each selected ward, 90 elderly individuals were identified through systematic random sampling using updated voter lists as the sampling frame.

Eligibility Criteria:-
Inclusion Criteria:
1. Age 60 years or above at the time of enrollment.
2. Continuous residency in the selected ward for a minimum of six months prior to the study.
3. Capacity to provide voluntary, written informed consent.
4. Sufficient cognitive orientation to comprehend and respond to assessment questions.

Exclusion Criteria:
1. Individuals who were completely bedridden or diagnosed with a terminal illness.
2. Those who declined participation or withdrew consent at any stage of the study.

Measures and Variables
Primary measures for this interaction analysis included:
1. Cardiovascular Function:
   - Static Measures: Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Pulse Pressure (PP = SBP - DBP).
   - Dynamic/Autonomic Measure: Heart Rate Variability (HRV) was derived from a 5-minute resting ECG recording. Time-domain indices analyzed were: Standard Deviation of NN intervals (SDNN, ms) and Root Mean Square of Successive Differences (RMSSD, ms). Frequency-domain analysis provided the Low Frequency/High Frequency ratio (LF/HF).
2. Respiratory Function: Assessed via portable spirometry. Key indices were: Forced Expiratory Volume in 1 second (FEV1, L), Forced Vital Capacity (FVC, L), and the FEV1/FVC ratio. Percent predicted values were calculated using GLI-2012 equations.
3. Cognitive Function: Evaluated using:
   - Mini-Mental State Examination (MMSE): A global cognitive screening tool (score 0-30).
   - Montreal Cognitive Assessment (MoCA): A more sensitive tool for detecting mild cognitive impairment (score 0-30).
4. Psychological Status: Measured using the 12-item General Health Questionnaire (GHQ-12) with Likert scoring (0-3 per item; total 0-36). Higher scores indicate greater psychological distress.
5. Covariates: Age, gender, years of formal education, socioeconomic status (SES), and lifestyle factors (physical activity, smoking status) were included as covariates in multivariate models.

Statistical Analysis:-
Data were analyzed using SPSS v25.0 and R software.
1. Descriptive Statistics: Means ± SD or medians (IQR) for continuous variables; frequencies for categorical variables.
2. Correlation Analysis: Pearson's correlation coefficient (r) was used for normally distributed variables; Spearman's rank (ρ) was used for non-normal distributions to examine bivariate relationships between physiological and cognitive/psychological variables.
3. Multiple Linear Regression: A hierarchical multiple regression model was constructed with MoCA score as the dependent variable. Blocks of predictors were entered sequentially: Block 1 (Demographics: age, gender, education), Block 2 (Cardiovascular: SBP, PP, SDNN), Block 3 (Respiratory: FEV1 % predicted), Block 4 (Psychological: GHQ-12 score). Assumptions of linearity, homoscedasticity, and normality of residuals were checked.
4. Group Comparisons: Participants were stratified by key morbidity status (e.g., Hypertensive vs. Normotensive; COPD vs. Normal spirometry). Group differences in cognitive and HRV indices were tested using independent t-tests or Mann-Whitney U tests.

5. Cluster Analysis: A k-means cluster analysis was performed using the standardized scores of four key variables representing different systems: SBP, FEV1 (% pred), MoCA score, and GHQ-12 score. The optimal number of clusters was determined using the elbow method and silhouette analysis. ANOVA and Chi-square tests were used to characterize the resulting clusters.
6. Significance Level: A p-value < 0.05 was considered statistically significant.

Ethical Considerations:-
The study was approved by the Institutional Ethics Committee.

Results:-

Table 1 show basic demographic details of participants. A total of 180 elderly individuals participated in the study. The average age of participants was found to be around 72 years.Around 54% participants were female. Table 2 shows correlation between across various systems. Cardiovascular measures showed significant negative correlations between systolic blood pressure (SBP) and pulse pressure (PP) with cognitive performance on the MMSE and MoCA, with the strongest association observed between PP and MoCA ($r = -0.30$, $p < 0.001$). Respiratory function, assessed via spirometry indices (FEV1, FVC, and FEV1/FVC), exhibited positive correlations with cognitive scores, wherein FEV1 demonstrated the most robust link to MMSE ($r = 0.25$, $p < 0.001$). Regarding psychological well-being, heart rate variability parameters (SDNN and RMSSD) were inversely associated with GHQ-12 scores ($r = -0.34$ and $r = -0.29$, respectively; both $p < 0.001$), suggesting reduced parasympathetic activity among individuals reporting higher distress.

The hierarchical multiple regression model (Table 2) explained 38.4% of the variance in MoCA scores (Adjusted $R^2 = 0.384$). Age and higher education (β value -0.32 and +0.28 respectively) were the strongest predictors. Cardiovascular and respiratory (SBP: $\beta = -0.21$ and FEV1: $\beta = +0.19$) functions emerged as significant independent physiological predictors. Psychological distress (GHQ-12 score: $\beta = -0.17$, $p=0.003$) also independently contributed to lower cognitive scores, even after accounting for all other factors.Table 3 shows cluster analysis of various group. It identified three distinct phenotypic clusters. Cluster 1: "Resilient Agers" (32.2%, n=58): Characterized by lower SBP, better lung function, highest cognitive scores, and lowest psychological distress. This group was younger and had higher education.Cluster 2: "Vascular-Cognitive Decliners" (41.1%, n=74): Marked by the highest SBP and PP, moderate lung function, significantly lower cognitive scores, and moderate psychological distress.Cluster 3: "Multisystem Compromised" (26.7%, n=48): Exhibited poor lung function (lowest FEV1), low cognitive scores, the highest psychological distress, and low HRV, despite having intermediate BP levels. This group had the highest proportion of smokers and sedentary individuals.

Discussion:-

This community-based study provides integrated evidence that aging in an urban Indian elderly population is characterized by clinically relevant interactions among cardiovascular, respiratory, cognitive, and psychological systems. Rather than functioning independently, these domains appear to influence one another in ways that shape distinct aging trajectories. The identification of multisystem phenotypes further supports emerging models that conceptualize aging as a network-level process rather than a collection of isolated organ failures [2,3].A key finding of this study was the inverse association between pulse pressure and cognitive performance, particularly MoCA scores. Pulse pressure is a recognized surrogate marker of central arterial stiffness [10]. Increased arterial stiffness permits excessive pulsatile flow to reach the cerebral microvasculature, contributing to endothelial injury, disruption of the blood–brain barrier, and white matter damage [5,11]. Our findings are consistent with the vascular hypothesis of cognitive aging and align with results from large population-based cohorts such as the Rotterdam Study, which demonstrated an association between elevated pulse pressure and increased dementia risk [12]. The persistence of this relationship after adjustment for age and education suggests that vascular stiffness may independently contribute to cognitive vulnerability, even in low- and middle-income country settings.

Respiratory function also showed a significant positive association with cognitive performance, with higher FEV1 values correlating with better MMSE and MoCA scores. These findings reinforce the concept of a lung–brain axis, wherein declining pulmonary function contributes to chronic hypoxia and systemic inflammation, both of which adversely affect neuronal integrity [6,13]. Hypoxia has been shown to impair hippocampal neurogenesis and promote neurodegenerative processes, while inflammatory mediators can cross the blood–brain barrier and activate microglial pathways implicated in cognitive decline [14]. In the present study, participants with spirometry-defined

COPD demonstrated poorer cognitive and psychological profiles, highlighting the broader systemic consequences of respiratory impairment. In the Indian urban context, widespread exposure to ambient and household air pollution may further amplify these effects [9].

Autonomic dysfunction, reflected by reduced heart rate variability, emerged as an important link between psychological distress and cognitive outcomes. HRV is a well-established marker of parasympathetic (vagal) activity and overall autonomic balance [15]. Chronic psychological stress and depressive symptoms are associated with reduced HRV, indicating sustained sympathovagal imbalance [16]. This imbalance may promote inflammation, endothelial dysfunction, and metabolic dysregulation, all of which adversely affect cardiovascular and brain health [7]. The independent association between GHQ-12 scores and MoCA performance observed in this study suggests that psychological distress may influence cognition through both direct pathways and indirect mechanisms mediated by autonomic and inflammatory processes.The cluster analysis revealed clinically meaningful phenotypes that underscore heterogeneity in aging trajectories. The "Vascular–Cognitive Decliners" cluster, characterized by elevated blood pressure and disproportionately lower cognitive scores, represents a subgroup likely to benefit from intensive vascular risk management. In contrast, the "Multisystem Compromised" cluster demonstrated poor lung function, high psychological distress, and markedly reduced HRV despite only intermediate blood pressure levels. This phenotype highlights the limitations of relying solely on traditional cardiovascular risk markers and suggests that combined respiratory, psychological, and lifestyle factors may drive vulnerability in a subset of older adults.Several limitations warrant consideration. The cross-sectional design precludes causal inference, and reverse causality cannot be excluded. Residual confounding by unmeasured factors such as nutritional status or subclinical cerebrovascular disease is possible. Nevertheless, the community-based design and integrated assessment of multiple physiological systems strengthen the relevance of these findings for real-world geriatric care in India.

Conclusion:-

The present study demonstrates that aging in urban Indian older adults is marked by interconnected declines across cardiovascular, respiratory, cognitive, and psychological systems. Measures of arterial stiffness, pulmonary function, autonomic regulation, and psychological distress were each independently associated with cognitive performance, suggesting that cognitive aging reflects broader systemic dysregulation rather than isolated brain pathology.

Recommendations:-

Future studies should use long-term designs to better understand cause-and-effect links between these body systems. Adding tests for inflammation, oxidative stress, and brain cell damage will help reveal the key processes involved. Our results strongly support testing new interventions. Researchers should trial combined programs, such as aerobic exercise to boost heart and lung health, mindfulness to ease stress and improve nervous system balance, plus cognitive training, to slow overall decline across systems.

Table 1: Stratified Distribution of Participants by Age, Gender, and Socioeconomic Status (SES) (n=180)

Characteristic	Category	n	%
Gender	**Male**	87	48.3
	Female	93	51.7
Age Group	**60-69 years**	54	30.0
	70-79 years	93	51.7
	≥80 years	33	18.3

Table 2: Correlation Matrix of Key Physiological and Psychological Variables (n=180)

Variable	SBP	PP	SDNN	FEV1	MMSE	MoCA	GHQ-12
SBP	1.00						
PP	0.82***	1.00					
SDNN (HRV)	-0.18*	-0.15*	1.00				

FEV1 (L)	-0.11	-0.09	0.22**	1.00			
MMSE	-0.28***	-0.26**	0.19*	0.25***	1.00		
MoCA	-0.32***	-0.30***	0.23**	0.27***	0.75***	1.00	
GHQ-12	0.12	0.10	-0.34***	-0.21**	-0.31***	-0.36***	1.00
*p<0.05, **p<0.01, ***p<0.001 (Pearson's r). SBP - Systolic Blood Pressure, PP - Pulse Pressure.							

Table 3: Hierarchical Multiple Regression Predicting MoCA Score (n=180)

Model Block & Predictor	β Coefficient	SE β	Standardized β	t-value	p-value
Block 1: Demographics					
Age	-0.15	0.03	-0.32	-5.33	**<0.001**
Gender (Female)	0.41	0.32	0.07	1.28	0.203
Education (Years)	0.23	0.05	0.28	4.98	**<0.001**
Block 2: +Cardiovascular					
Systolic BP	-0.05	0.01	-0.21	-3.74	**<0.001**
Pulse Pressure	-0.02	0.02	-0.06	-1.05	0.295
SDNN (HRV)	0.01	0.01	0.08	1.42	0.158
Block 3: +Respiratory					
FEV1 (% Predicted)	0.03	0.01	0.19	3.12	**0.002**
Block 4: +Psychological					
GHQ-12 Score	-0.35	0.12	-0.17	-2.98	**0.003**
Model Summary: $R^2 = 0.402$, Adjusted $R^2 = 0.384$.					

Table 4: Characteristics of Phenotypic Clusters Identified by K-means Analysis

Characteristic	Cluster 1: Resilient Agers (n=58)	Cluster 2: Vascular-Cognitive Decliners (n=74)	Cluster 3: Multisystem Compromised (n=48)	p-value (ANOVA/χ^2)
Age (years)	68.9 ± 6.5	73.8 ± 7.9	75.2 ± 8.8	<0.001
SBP (mmHg)	132.4 ± 12.1	151.8 ± 15.2	140.5 ± 17.3	<0.001
FEV1 (% Pred)	89.2 ± 10.5	76.8 ± 11.3	62.1 ± 14.5	<0.001
MoCA Score	26.1 ± 2.1	21.3 ± 3.2	19.0 ± 3.8	<0.001
GHQ-12 Score	1.5 ± 1.0	2.9 ± 1.8	4.5 ± 2.4	<0.001
SDNN (ms)	125 ± 38	102 ± 35	88 ± 31	<0.001
% Current Smoker	10.3%	18.9%	31.3%	0.024

Table 3: Prevalence of Key Morbidities among Study Participants (n=180)

Morbidity	Overall Prevalence n (%)	95% CI	ByGender Male (%)	Female (%)	p-value*
Hypertension	126 (70.0)	63.0–76.3	48.3	45.1	0.667
Uncontrolled HTN*	84 (46.7)	39.3–54.2	48.3	45.1	0.667
COPD (Spirometry)	31 (17.1)	12.1–23.4	19.0	15.1	0.483
Cognitive Impairment	48 (26.5)	20.4–33.6	24.1	29.0	0.456
Psychological Morbidity (GHQ-12≥3)	60 (33.3)	26.6–40.7	27.6	38.7	0.112
Multimorbidity (≥2 conditions)	106 (58.9)	51.4–66.0	56.3	61.3	0.502
2 conditions	62 (34.4)	27.7–41.8			
≥3 conditions	44 (24.4)	18.5–31.4			
*Chi-square test for gender difference.					

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