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STUDYING THE RELATIONSHIP BETWEEN INSULIN GROWTH FACTOR 1, C - REACTIVE PROTEIN AMONG DIABETIC FRAIL ELDERLY

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Frailty, CRP, IGF-1, Diabetes, Elderly.

Abstract

Objective: to study the relationship between Insulin Growth Factor 1(IGF-1) and C - reactive protein (CRP) among diabetic frail elderly

Methods: A case control study has been carried on 90 elderly aged 60 years and over, collected from (Mansora university hospital & community dwelling elderly) during the period January 2015 - July 2015. Subjects were divided into: Control group of 30 healthy elderly and cases group: of 60 frail elderly which is furtherly subdivided into two subgroups: frail with diabetes and frail without diabetes. Subjects were subjected to comprehensive geriatric assessment and study of osteoporotic fractures (SOF) index for assessment of presence of frailty.

Results: IGF-1 level was significantly lower among the frail patient. Also, IGF -1 level was significantly lower among diabetic frail elderly. In addition, CRP level, significantly higher among frail elderly but there was no significant statistical difference between the frail diabetic & frail non diabetic as regards the CRP level.

Conclusion: Frail elderly had a lower IGF-1 level and a higher CRP level in compare with control participant. Also, diabetic frail elderly had significantly lower IGF-1 level compared to the non-diabetics. However there was no difference between CRP level among diabetic and non-diabetic frail elderly.

Introduction

Frailty is a common term used to indicate that older adults at increased risk for many adverse outcomes like onset of disability, morbidity, or mortality or developing a failure to integrate good responses against stress [(1)]. Although there is a universal recognition of the frailty syndrome by most of geriatrician, there is still a lack of consensus definition and clinical assessment tools. This failure is one of the major barriers for efficient preventive measures [(1)]**.** Before planning appropriate management for frailty causes, identification of frailty with an appropriate tool should be done first. This assessment will be extremely heterogeneous without consensus on the definition and components of frailty [(2)]**.**

According to the physiological domains from previous studies and suitability of assessment of components in a clinical practice, a simple frailty index was proposed using three components, (SOF) index [(3)]**.** ***Ensrud***[(3)]have defined frailty according to SOF by presence of two or more of the following three components at the second examination:
(1) Weight loss (irrespective of intention to lose weight) of 5% or more between the baseline and second examination (mean years between examinations 3.4 ± 0.5)
(2) Inability to rise from a chair five times without using the arms

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(3) Poor energy as identified by an answer of ‘‘no’’ to the question ‘‘Do you feel full of energy?’’ on the Geriatric Depression Scale (GDS)
Persons who have Diabetes Mellitus (DM) tend to have an accelerated aging process that makes them at a higher risk for developing frailty at an earlier age [4]

The objective of this study is to assess the relationship between IGF-1, CRP and diabetes among frail elderly.

Materials and methods

Our study enrolled 90 elderly aged 60 years and over, (49 males &41 females); collected from Mansora university hospital out-patient clinics & community dwelling elderly during the period January 2015 - July 2015. Subjects were divided into:
A) Control group: composed of 30 healthy elderly
B) Cases group: composed of 60 frail elderly “according to SOF index”. Then cases furtherly subdivided into two subgroups:

- Group (1) Frail elderly with DM
- Group (2) Frail elderly without DM

Each participant was subjected to the following:
-Informed oral consent.
-Personal history & special habits of medical importance.
-List of the current diseases & medication taken by the patients.
-Measurement of the arterial blood pressure using the mercury sphygmomanometer after 10 minutes rest, in adequate room temperature while the patient is lying flat.
-Body Mass Index (BMI) was calculated by determining the ratio between weight and the square of the height (expressed in kg/m2)
-Comprehensive geriatric assessment, which includes: complete physical examination, MMSE, GDS and activity of daily living
-After exclusion of diseases that may lead to change in CRP level as: [myocardial infarction, infections, trauma, acute and chronic inflammations, collagen diseases, chronic liver diseases and drugs as statins & aspirin] and disease that affects IGF-1 level as [GH disorders (acromegaly and hypopituitarism), chronic Liver disease, chronic renal failure, hypothyroidism and patient taking estrogen], a venous blood sample (5cubic centimeter) was taken from the participants & centrifuged, then plasma is stored in the freezer. After collection of the samples, they were analyzed for: serum IGF-1 was assayed by Enzyme Linked Immunosorbent Assay (ELISA) technique using assay max human IGF-1 ELISA kits supplied by Assaypro LLC (made in United States) & serum high sensitive CRP was assayed by turbidemetric method supplied by Biosynthesis (made in Spain)
-The normal reference ranges of these kits were: IGF-1 (30-300 ng/ml) & CRP “high sensitive” (less than 3 ug/ml)
-Statistical analysis (using IBM SPSS software package version 20.0) included descriptive statistics for normal and abnormal findings. P value was considered statistically significant if it was <0.05

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Results and discussion

Table 1. : Comparison between the case subgroups regarding the demographic data

	Cases						
	Total (n=60)		With DM (n=30)		Without DM (n=30)		P
Age (years) -Min-Max -Mean + SD -Median	61-92 72.75+8.5 70.5		62-87 71.17+7.61 68.5		61-92 74.33+9.15 73		0.086
Sex	No.	%	No.	%	No	%	
-Male	38	63.3	20	66.7	18	60	0.592
-Female	22	36.7	10	33.3	12	40	
Special Habits	No.	%	No.	%	No.	%	
-Non-Smoker	42	70.0	20	66.7	22	73.3	0.779
-Ex-Smoker	12	20.0	6	20.0	6	20.0	
-Smoker	6	10.0	4	13.3	2	6.7	

P: p value for comparing between 2 subgroups of the cases

Table 2. Comparison between the studied groups regarding the presence of cognitive impairment using MMSE & the presence of depression using GDS

	Control (n= 30)	Cases			
		Total (n= 60)	With diabetes (n= 30)	Without diabetes (n= 30)	p
MMSE (Min. – Max). MMSE (Mean ± SD). MMSE (Median)	21.0 – 30.0 28.70 ± 1.76 29.0	17.0 – 29.0 24.87 ± 2.55 25.0	17.0 – 29.0 25.10 ± 2.82 26.0	19.0 – 28.0 24.63 ± 2.28 25.0	p= 0.280
$p_{cont.}$		<0.001*	<0.001*	<0.001*	
GDS (Min. – Max). GDS (Mean ± SD). GDS (Median)	1.0 – 7.0 2.03 ± 1.19 2.0	1.0 – 12.0 4.92 ± 2.29 4.0	3.0 – 11.0 4.93 ± 1.98 4.0	1.0 – 12.0 4.90 ± 2.59 4.0	p= 0.678
$p_{cont.}$		<0.001*	<0.001*	<0.001*	

P: p value for comparing between 2 subgroups of the cases
$P_{cont.}$: p value for comparing between control and each other group

Table 3. Comparison between the studied groups regarding the IGF-1 & CRP level

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	Control (n= 30)		Cases					
			Total (n= 60)		With diabetes (n= 30)		Without diabetes (n= 30)		p
	No.	%	No.	%	No.	%	No.	%	
IGF-1 (Min. – Max).	24.0 – 140.0		18.0 – 148.0		18.0 – 60.0		20.0 – 148.0		P <0.001*
IGF-1 (Mean ± SD).	68.13 ± 33.90		49.23 ± 35.64		29.17 ± 9.89		69.30 ± 40.67		
IGF-1 (Median)	52.0		32.0		26.0		54.50		
$p_{cont.}$			0.001*		<0.001*		0.941		
CRP (Min. – Max).	0.50 – 5.50		0.50 – 39.50		0.50 – 39.50		0.50 – 12.50		p= 0.778
CRP (Mean ± SD).	1.73 ± 1.17		4.43 ± 6.16		5.25 ± 7.98		3.60 ± 3.48		
CRP (Median)	1.50		2.25		2.0		2.50		
$p_{cont.}$			0.020*		0.036*		0.055		

P: p value for comparing between 2 subgroups of the cases
$P_{cont.}$: p value for comparing between control and each other group

Discussion

Frailty is an important geriatric syndrome associated with decline in physiologic reserve which may increase susceptibility for adverse health outcomes [7]. Diabetes causes premature ageing and also it's a cause of unsuccessful ageing. Furthermore it is associated with increased disability, morbidity, mortality.[8]. Morley[9] proposed that diabetes in elderly may be associated with frailty at an earlier stage than those non-diabetics.

The current study was conducted to study the relationship between IGF-1, CRP, depression, cognitive impairment and diabetes in frail elderly patients. Furthermore, the current study reported that there was highly significant statistical difference as regards the age between the case & control groups as the frail participant older than the control group. This results match with Song [10] who reported that frailty increased steadily with age: 65-69 years: 4%; 70-74 years: 7%; 75-79 years: 9%80-84 years: 16%; >85 years: 26%. Also, Fried [11] reported that frailty increases with age from 3.9% in the age-group 65–74 years to 25% in the age group older than 85 years. On the other hand there's no significant statistical difference between the frail diabetic & frail non diabetic subgroups as regards the age and sex.

The relation between frailty and cognitive power was studied and it was found that there was a significant statistical difference as regards the cognitive power between the two groups in which the frail group has a poor performance in the MMSE. This matches with Brigola[12], they published a review article concluded that there was a link between cognition and frailty in elderly. A total of 19 studies –most of them using MMSE- were selected for their review, majority of them are Brazilian. All of the studies established a link between cognition and frailty.
Also we agreed with Samper-Ternent[13]. They studied the link between frailty and cognitive function over time in older Mexican Americans. They include 1370 Mexican-American men and women aged 65 and older using MMSE as a screening test for cognitive impairment and they found that frail subjects had greater cognitive decline over 10 years than non-frail subjects and they explained this as in some dementias the accumulation of neural plaques and fibrillary tangles is involved in the etiology of the decline of cognitive impairment and it had been shown that alterations in these areas of the brain are associated with modifications in frailty component as weight loss and slowing of the gait. On the other hand there's no significant statistical difference between the frail diabetic & frail non diabetic subgroups as regards the cognitive impairment. However it was noticed in the current study that the

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frail diabetic patient have a statistically significant poor cognitive power in compare with frail non diabetic patient as DM is a well-established risk factor for development of dementia [14]

Another point of study which is the depression; using the GDS as a screening tool, the current study showed that there was a highly significant statistical difference as regards the presence of depression between the case & control groups. Moreover it was noticed that the GDS score among the control subjects is significantly lower in compare with frail patients. On the other hand there's no significant statistical difference between the frail diabetic & frail non diabetic subgroups as regards the GDS. This results matched with Buigues[15]. They performed searches in several databases papers published between November 2003 to February 2014 about frailty syndrome and depression in people aged 65 and older published. Finally they found that there was a significant proportion of frail older having depression. They found that the co-occurrence of both frailty and depression among people aged 65 and over has only recently started to be investigated from 2009 and most of studies found that it was around 4% to16% of frail individuals aged 60 and over had serious depression. However, this percentage increases to 35% when an older (aged 75 and over) population is selected or when considering frail men.

Another point of study is the laboratory investigation. We investigated the IGF-1 level and it found that there was a highly significant statistical difference between the case & control group in which the IGF-1 level was found to be lower among the frail patient. This matched the results of Yeapetal [16] who studied the relation between IGF level and frailty. They conducted an observational study of 3447 community dwelling men aged 70–89 years assessed in 2001–04 by IGF-1 level and 1654 reassessed in 2008–09. They had found 527 frail elderly in their study, and they found that the frail elderly had a significantly lower IGF than non-frail elderly and the current study matches these results. Recently, Mohamad [17] studied one hundred elderly males in a study to measure IGF-1. They divided them into two groups, frail group (50 patient) and robust group (50 patient) based on SOF frailty index. Anthropometric measures, femoral BMD, and serum IGF-1 level were measured and the concluded that the IGF-1 level was significantly lower in the frail males and this agree with our study. Furthermore, the current study compared the level IGF-1 among frail diabetic and frail non diabetic patients and also there was a highly significant statistical difference between the two subgroups as regards the level IGF, in which it was significantly lower among frail diabetic patient.
Also, this is matched with the study conducted by Aneke-Nashm [18]. They studied the change of IGF level among patients with type II DM. and they found that patients with type II DM had a lower IGF level

Conclusion

The conducted study concluded that the frail elderly had a lower IGF-1 level and a higher CRP level in compare with control participant. Diabetic frail elderly had significantly lower IGF-1 level compared to the non-diabetics. However there was no difference between CRP level among diabetic and non-diabetic frail elderly. Both depression and impairment of the cognitive power are significantly higher among frail elderly. On the other hand presence of diabetes doesn't increase the depression or cognitive impairment among frail elderly

References

1. Morley JE, Haren MT, Rolland Y et al. "Frailty". Med Clin North Am;90:837-847. 2006
2. Gill TM, Gahbauer EA, Han L, et al. "Trajectories of disability in the last year of life. New England J of Medicine"; 362(13):1173–1180. 2010 [PubMed: 20357280]
3. Ensrud KE, Ewing SK, Taylor BC et al. "Comparison of 2 frailty indexes for prediction of falls, disability, fractures, and death in older women". Arch Intern Med;168:382–389.2008
4. Mazza AD, Morley JE."Update on diabetes in the elderly and the application of current therapeutics". J American Med Dir Association;8:489–492.2007
5. Kotz S, Balakrishnan N, Read C et al. "Encyclopedia of statistical sciences". 2nd ed. Hoboken, N.J.: Wiley-Interscience; 2006.
6. Kirkpatrick LA, Feeney BC. A simple guide to IBM SPSS statistics for version 20.0. Student ed. Belmont, Calif.: Wadsworth, Cengage Learning; 2013.
7. Chen X, Mao G, Leng S; "Frailty syndrome: an overview, Clinical Interventions in Aging":9 433–441.2014

June 2016; 3(6) ISSN: ISSN: 2349-5340
DOI: 10.5281/zenodo.55184 Impact Factor: 3.052

8. Sinclair AJ, Meneilly GS."Type 2 diabetes mellitus in senior citizens. In: John Pathy MS, Sinclair AJ, Morley JE (eds)". Principles and Practice of Geriatric Medicine. 4 ed. Chichester: Wiley,:1431-45.2006
9. Morley JE, Kim MJ, Haren MT. "Frailty and hormones". Rev EndocrMetabDisord;6:101-108.2005
10. Song X, Mitnitski A, Rockwood K. "Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation". J American Geriatric Society; 58(4):681–687. 2010 [PubMed: 20345864]
11. Fried LP, Ferrucci L, Darer J, et al"Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care". J Gerontology ABiolSci Med Sci.;59: 255–263.2004
12. Brigola A G, Rossetti E S, Santos B R, et al, "Relationship between cognition and frailty in elderly", A systematic review, Dement Neuropsychol June; 9(2):110-119. 2015
13. Samper-Ternent R,Snih S A, Raji M A, Markides K S et al, "Relationship Between Frailty and Cognitive Decline in Older Mexican Americans", J American Geriatrics Society, vol56 Issue 10 pages 1845–1852, October 2008
14. Ninomiya T. "Diabetes Mellitus and Dementia", Springer Science+Business Media New York 2014, CurrDiab Rep 14:487. 2014
15. Buigues C, Padilla C , Garrido J F, et al. "The relationship between depression and frailty syndrome," a systematic review, Aging & Mental HealthVol 19, Issue 9, pages 762-772, 2015
16. Yeap B B, Paul Chubb S A, Derrick L K, et al, "Associations of insulin-like growth factor-I and its binding proteins and testosterone with frailty in older men", Clinical Endocrinology78, 752–759. 2013
17. Mohamad M I and Khater M S, "Evaluation of insulin like growth factor-1 (IGF-1) level and its impact on muscle and bone mineral density in frail elderly male", Archive of Gerontology and Geriatrics, Vol 60, Issue 1, January-February, 124-127. 2015
18. Aneke-Nash C,Parrinello C M,Rajpathak S Net al, "Changes in Insulin-Like Growth Factor-I and Its Binding Proteins Are Associated with Diabetes Mellitus in Older Adults", J of the American Geriatrics Society, volume 63 , issue 5 pages 902–909, May 2015