Luteinizing Hormone in Frail Elderly Individuals

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Abstract:
Background: The term "frailty" has been used clinically as a global concept to describe a condition, common in the old, of impaired strength, endurance, and balance, vulnerability to trauma and other stressors, and high risk for morbidity, disability, and mortality. A variety of factors may contribute to frailty or to one or more of its specific features. These include inflammatory, musculoskeletal, cardio respiratory, metabolic, hematologic, neurologic, immunologic and endocrine factors. Hormones important to the development of frailty that has been proposed include testosterone, luteinizing hormone (LH) and dehydroepiandrosterone (DHEA). **Objective:** to study the association between LH level and frailty among the elderly **Method:** A case control study was carried out. The case group included 80 Frail elderly subjects selected according to the American Geriatric Society Criteria; whereas 80 non-Frail elderly subjects were selected as the control group. Each participant was subjected to Comprehensive Geriatric Assessment and laboratory assessment of luteinizing hormone. **Results:** LH level was lower in frail subjects compared to non frail. Lower levels were significantly correlated with increased degree of dependency in both frail males and females. **Conclusion:** Luteinizing hormone level was lower among frail elderly. Further studies are needed to confirm such an association and to plan clinical practice accordingly.
Key words: Frailty, Luteinizing hormone, independence.

Introduction:

The term frailty is frequently used within the geriatrics world to describe patients who are in poor overall health, vulnerable to the ill effects of a variety of environmental stressors, and are further at high risk for worsened morbidity, worsened disability, and mortality. Clinical researches demonstrate that these patients, are heavy users of medical services, and have a tough lot in life [(1)].

Despite the ability to conceptualize and study these patients in the aggregate, a simple consensus definition and criteria for frailty has remained elusive. The elusiveness of the definition of frailty reflects not only the challenges in defining a clinical syndrome where the exact etiology and path physiology are unknown but also the challenges of defining the boundaries of a syndrome that has medical, functional, and social components[(1)] .

However, researchers have, for the most part, disentangled frailty from disability in basic activities of daily living (ADL) with many authors considering the

defect in ADL a major component of clinical criteria of frailty[2] .
There is also a strong rationale for the inclusion of additional components such as cognition and mood, which may be affected by the same biological processes that lead to the manifestations of "physical" frailty. Several mechanisms have been hypothesized to have an important role in the development of frailty, including inflammation, coagulation and oxidative stress .Many authors implicate age-related hormonal changes to be directly or indirectly involved in the development of the frailty syndrome. Alterations in hypothalamic- pituitary-gonadal, hypothalamic-pituitary-adrenal (HPA) and growth hormone- insulin growth factor I (GH-IGF-I) axes that accompany aging have been associated with frailty [3] .
Hormones that have been proposed to be important to the development of frailty include; testosterone, luteinizing hormone and dehydroepiandrosterone (DHEA) [4] .
As we age, changes naturally occur in the way that body systems are controlled. Some target tissues become less sensitive to their controlling hormone. The amount of hormones produced may also change. Hormones are also broken down (metabolized) more slowly.
Blood levels of some hormones increase, some decrease, and some are unchanged.
A number of studies have assessed the hormonal changes associated with frailty including Luteinizing hormone (LH) with conflicting results.

Aim of the study: the aim of the current study is to evaluate the association between LH level and frailty in the elderly.

Methods

Participants and study design

This was a case control study enrolling 160 elderly subjects 60 years and above all being recruited from outpatient clinics of the Geriatrics and Gerontology department of Ain Shams University Hospitals.
The selected group was subdivided into 2 groups:
First group: 80 Frail elderly subjects selected according to the American Geriatric society criteria [5] as follows:

- Individuals who have severe disability in two or more of the following domains or moderate disability in at least three or more of these domains: physical health, mental status, functional status, socio-economic status and residential environment; or
- Individuals who are disabled in two instrumental activities of daily living (IADL) and one ADL; or
- Individuals aged 85 years or older; or
- Older individuals who are homebound; or
- Older individuals with mental disorders such as dementia; or
- Older individuals with communication disorders; or
- Individuals with significant sequelae of multiple chronic conditions such as arthritis, hypertension, heart disease, diabetes, osteoporosis, fracture, stroke, cancer (currently active), dementia, and Parkinson's disease

Second group: 80 non-frail elderly as control group

All participants were subjected to comprehensive geriatric assessment which includes:

- Full history taking and physical examination.
- Assessment of the cognitive status by using the Arabic version [6] of Mini mental state examination (MMSE) [7]**.** MMSE is one of the most commonly used cognitive screening measures being quick and easy to administer. It includes specific questions related to attention, orientation, memory, calculation and language.
- Assessment for depression by using the Arabic version [8] of the Geriatric Depression scale (GDS) [9]**.** It is the 15-item GDS which is well –validated tool often used to screen for depressive symptoms in older individuals. This measure is scored based on a 15-points scale and impairment is indicated by a score of 5 or higher.
- Assessment of the daily living activity by using: activity of daily living (ADL) [10] and instrumental activity of daily living (IADL) [11] **.**Questionnaire of both ADL and IADL are informant- based assessment of functional disabilities. The ADL questionnaire measures functionality in 5 areas: bathing, toileting, grooming, dressing and eating. While the IADL questionnaire measures functionality in traveling, shopping, house work, managing finances, using the telephone and taking medications.

Lab testing

Serum luteinizing hormone was measured (in mIU/ml) using sandwich enzyme immunoassay technique (Human luteinizing hormone ELISA kit) the test is based on phase enzyme – linked immunosorbent assay

Ethical considerations

The study was approved by the Ethical Committee of the Faculty of Medicine, Ain Shams University. Informed consent was obtained from participants, their nearest relatives, or both depending on the patient's cognition.

Statistical analysis

Data collected was revised, coded, tabulated and introduced to PC for statistical analysis. All data manipulation and analysis was performed using the 17th version of SPSS (Statistical Package for Social Sciences). Qualitative data was presented in the form of frequency tables (number and percentage). Quantitative data was presented in form of mean ± standard deviation and range. Pearson Chi-squared was used with correction to test the association between 2 qualitative variables. Independent sample-t test was also used to compare two groups with quantitative continuous variables. P value was always set as significant at 0.05.

Results:

The current study enrolled 160 elderly subjects 60 years and above, 80 frail elderly and 80 sex and age matched non-frail elderly totally independent in ADL, IADL and had MMSE >24 . The mean age of the studied group was 67.86±6.5 years.

As regards the mean LH level in males there was no significant difference statistically between cases (10.2mIU/ml) and controls (10.5mIU/ml). There was a lower mean LH level among female cases (22.6mIU/ml) compared to female

controls (38.4 mIU/ml) and the difference was significant statistically (P<0.05). (Table 1)

Table (1) Comparison between frail individuals and controls as regards mean LH level:

	Frail Mean SD	Non-frail Mean SD	t	P-value
Males	10.2 11.7	10.5 6.7	0.1	**>0.05 NS**
Females	**22.6 31.0**	**38.4 26.6**	**2.6**	**<0.05 Sign**

There was highly significant negative correlation between LH level and degree of dependency in ADL with lower levels of LH was significantly correlated with higher degree of dependency in ADL in frail female individuals, while no other significant correlation could be detected between LH level and any of the studied parameters including age, male gender, depression and cognitive impairment (Table 2)

Table(2) Correlation between LH level &Age, ADL, IADL, MMSE and GDS score among frail individuals.

	Males r P-value	Females r P-value
Age	0.86 0.50	**-.060 0.60**
ADL	-0 .241 0.05	**-0.399 0.00**
IADL	-0.234 0.05	**-0.389 0.00**
MMSE	0.140 0.25	**0.155 0.13**
GDS	**0.001 0.99**	**-0.141 0.17**

In studied group, (57.5%) of frail patients had Hypertension, (36.3%) had ISHD, (27>5%) had chronic liver diseases, (18.8%) had osteoporosis and (46.3%) had Diabetes mellitus but the difference was not statistically significant, while (22.5%) had cerebrovascular stroke but the difference was highly statistically significant (Table 3)

Table(3) Comparison between the two groups as regards chronic diseases:

	Frail	Non-frail	X^2	P
Hypertension	N=46 57.5%	N=51 63%	0.6	**>0.05 NS**
Osteoporosis	N=15 18.8%	N=24 30.0%	2.7	**>0.05 NS**
DM	N=37 46.3%	N=29 36.3%	1.6	**>0.05 NS**
ISHD	N=29 36.3%	N=28 35%	0.02	**>0.05 NS**
Cerebro-vascular stroke	N=18 22.5%	N=4 5%	10.3	**<0.01 HS**
Chronic liver	N=22 27.5%	N=21 26.3%	0.03	**>0.05 NS**
Renal impairment	N=14 17.5%	N=4 5%	6.2	**<0.05 NS**
Anemia	**N=10 12.5%%**	**N=8 10.0%**	**0.2**	**>0.05 NS**

Discussion:

Frailty is considered highly prevalent in old age and to confer high risk for falls, disability, hospitalization, and mortality. Frailty has been considered synonymous with disability, co morbidity, and other characteristics, but it is recognized that it may have a biologic basis and be a distinct clinical syndrome [(12)] **.**

A number of studies have assessed the hormonal changes associated with frailty including LH. There was a great conflicting results as regards LH level in

elderly in general and its relation to frailty which may be explained by the complexity of regulatory mechanisms of the hypothalamic –pituitary gonadal axis which highly altered with age, in addition to the wide variability in the interpretation of the nature of frailty. Frailty criteria give heterogeneous results when applied in clinical practice. The prevalence of frailty in a sample of 125 elderly people ranged from 33% to 88%, depending on the criteria used [(13)]**.**

A study found that serum LH levels significantly increase in independently living elderly men aged 73-94 years and positive significant relation existed between LH level and Stanford Modified Health Assessment Questionnaire (MHAQ) score as a parameter of frailty in which high score means low ability [(14)].

On the other hand, another study found Frailty index to be associated with increase in LH [(15)].

In the current study, LH level was lower among the frail elderly but with statistically significant difference among females only.

In a study conducted **a** group of 112 non frail postmenopausal women (mean age 67.6, range 50-88 years) was evaluated, they concluded that there is highly elevated postmenopausal level of LH hormone [(16)].

Although another study found that the level of Luteinizing hormone (LH) increase with age**,** [(17)] but the current study did not find correlation between the level of LH and age. Narrow age range of the studied group can explain such variation in results.

Similarly**,** another study found that LH did not change among age groups [(18)].

Studying the association between LH level and other studied parameters of frailty demonstrated that there was negative correlation between LH level and ADL and IADL statistically significant among frail females but not among males.

A study done found that frailty among 4,000 community dwelling elderly men and women over 65 years to be associated with physical inactivity [(19)]

In the current study there was no significant correlation between LH level and cognitive impairment (MMSE) in both males and females frail elderly. In a study done [(20)] in which patients were diagnosed on clinical grounds and screened by the mini mental score examination (MMSE), and LH was measured; the results showed that there was no significant difference in the level of LH hormone between cases and controls,

Also there was no significant correlation between LH level and depression (GDS) in both males and females frail elderly but this was not the case in a study done [(21)] where they measured serum LH in 46 postmenopausal frail female and matched normal controls, and they showed high LH concentrations in depressive females and positive correlation between the LH measures and severity of depression.

In the current study, 38.8% of frail cases had more than 3 co morbidities, As regard major geriatric syndromes cerebrovascular stroke was more among frail patients and the difference was statistically significant while Hypertension, osteoporosis and ISHD there was no statistical significant difference between the 2 groups.

Studies assessing the association of LH with diseases found contradicting results. LH was found to be higher among hypertensive thrombotic males[(22)] and among non frail men with osteoporosis[(23)]. On the contrary, Wranicz et al; (2005) suggested high level of LH to be protective against coronary artery disease [(24)].

Conclusion and Recommendation:

Based on the results of the current study, lower level of luteinizing hormone is significantly correlated with degree of dependency and no other significant correlations with any other studied parameters of frailty had been detected.

One of the limitations of the current study is the use of clinical rather than path-physiological definition of frailty, so further studies using path physiological definitions is warranted to clarify this topic and to put down definite criteria of frailty.

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