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Impact Of Environmental Factors And Lipid Imbalances On Hormonal Levels And Male Fertility In Older Individuals

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Abstract:
Background: A healthy lipid profile,normal Melatonin and prolactin levels is associated with healthy testosterone levels and male fertility. However, research on the exact relationship between lipid profiles, testosterone, Melatonin, Prolactin and male fertility is ongoing, with some studies showing correlations while others do not.
Aims and objective: A cross sectional study was carried out in groups of people living in Hunza valley and plain land of Lahore, Punjab to find out the effect of climate/environment on the lipid profile, Melatonin, prolactin and male fertility.
Material and Methods: Study included 50 subjects from Gilgit and 50 subjects from Lahore. Age of both groups was above 65 year. Both groups of subjects apparently had no disease. Study duration was eight months. The questionnaire encompassed demographic details (such as gender, and age), location information, medical history and was filled by each group of people. Blood sample of both groups were drawn to estimate the level of total / free testosterone (testosterone Elisa kit ADI. 900-065 by ENZO) and lipid profile, Melatonin and prolactin by technique of ELISA. Levels of lipids were estimated by standard kits of Radox bearing code LE2670
Results: Majority of the Hunza group used naswar(Quid) as compared to people of Punjab smoked cigarettes. Fertility rate appears to be high in Hunza group who were using mediterranean diet compared to Punjab group. Level of testosterone is non-signifciantly higher in Hunza group as compared to their counterparts in Punjab group. Lipid profile was however significantly higher in Punjab group as compared to men above 65 years in Hunza group.
Conclusion: As compared to people living in land area (Lahore, Punjab), high level of testosterone, Melatonin whereas with low levels of lipid profile and prolactin was observed in group of people living in hilly areas. Multi-centric researches are required to further explore the relationship of fertility with lipid profile, testosterone level and climate /environment in detail to reach better conclusion.

Key words: serum testosterone, lipid profile, Prolactin, melatoninfertility, hilly area .

Introduction:
Getting older is a unidirectional, essential process occurring in all cells and characterized by functional decline related to an increased risk of morbidity and mortality. [1,2]. People age at different rates and this diversity is the result of the cumulative impact of advantage and disadvantage within the physical and social environments they live in. [3]. As estimated by the World Health Organization, only as less as approximately 25% of the diversity in longevity is explained by genetic factors, while the other 75% is largely the result of the impact of our interactions with environments and exposures [4]. It is a major challenge to link environmental factors to specific cellular processes due to the complexity of the interaction, the long-term efficacy, multifaceted interactions, interference of demographic change and environmental exposure is potentially the modifiable risk factors for different diseases, the identification of such factors is a major strategy in lowering the burden of disease in elderly people [5].
The trans-National Institutes of Health Geroscience Interest Group (GSIG) has identified a set of seven highly intertwined processes at the core of age related diseases(ARD) including dementia, cardiovascular diseases, type 2 diabetes, hypertension, osteoporosis and may be infertility. Theincrease risk of ARDs and geriatric syndromes is dependent on molecular andcellular processes that are affected by both genetic and environmental factors. [6]
The ecological environment encompasses abiotic (soil, air and water) and biotic factors (microorganisms). These factors trigger mutations, pathologies, and tissue abnormalites.[7]Air pollution is a worldwide health problem with bad effects on human health in middle and developed countries [8]. In Asian developing countries people make use of residential energy as (heating purposes and for cooking) which then leads to a major risk to human health causing number of diseases like respiratory diseases which then alters oxidative status, increases heart diseasesas well as raises the problems of infertility[9].
Climate (assessed through temperature, humidity, atmospheric pressure etc) directly affects public health as exposure to ambient temperature which has an immediate/ strong impact on people's health. Increasing heat waves may rise the risk of cardiovascular problems, pulmonary disruptions and cerebrovascular deaths. [10]
Throughout the process of civilization, humans have built artificial, non-natural environments to protect themselves from natural threats and created new anthropogenic risk to human health such as pollution, noise andover crowding.[11]People who are residing in hilly areas are more into physical activities and that is very useful for levels of serum insulin, insulin-related pathways and inflammation[12],whereas those who are living in land areas and especially city side either do not get time for physical activities or most of their time is spent in sedentary chores.that is one reason that most men even above 65 years in

Hunza valley are more physically active and robust as compared to the ones living in Punjab. Additionally, physical activity is related with a low risk of psychiatric issues in older age such as cognitive impairment and dementia possibly due to improved mechanisms of neural plasticity stimulated by regular physical activity[13,14].

Moreover,Nutrition plays a major role in healthy ageing.The optimal nutrition of people from northern areas of Pakistan is Mediterranean diet, characterized by a balanced combination of fruit, vegetables, fish, cereals and polyunsaturated fats, meat mostly mutton ,fish and dairy products. These combinations make the perfectdiet to preserve health and improve longevity[15].

In our study we researched on lipid profile and testosterone in men from Hunza and Punjab age 65 years and above and compared their parameters.it is seen from many studies that healthy lipid profile is associated with good testosterone levels and male fertility However, further research on the exact relationship between lipid profiles, testosterone, and male fertility is ongoing, with some studies showing correlations while others do not. Testosterone levels are closely related to the development of the male reproductive system and male reproductive function[16]. Disturbed lipid metabolism may inhibit the synthesis of testosterone synthesis, resulting in limited spermatogenesis. Lipid homeostasis is indistinguishably linked to both semen parameters and levels of reproductive hormone [17].

Understanding and confirming healthy aging is important as the life span of human increases continually. It is a need to understand the role of environmental exposures in the development of aging-related issues like cardiovascular disease, fertility rate and dementia

Material and Methods

A cross-sectional study was carried out to compare the health status of people living in hilly area like Gilgit (healthy diet and healthy environment) and the people living in plane areas like Lahore. Study included 50 subjects from Gilgit and 50 subjects from Lahore. Age of both groups was above 65 year. Both groups of subjects apparently had no disease. Study duration was eight months. The questionnaire encompassed demographic details (such as gender, and age), location information, medical history etc and it was filled by each group of people. Letter of consent was taken from each subject. Study was approved from Ethical Board of IMBB department, University of Lahore---Lahore Pakistan. Blood sample of both groups were drawn to estimate the levels of total / free testosterone and lipid profile (Cholesterol, lipoproteins HDL and)of ELISA. Levels of lipid profile was estimated by standard kits of Merck.

Statistical Analysis: Data was analyzed by SPSS 21. Demographic characteristics of both groups was presented in percentages. Levels of lipid parameters (cholesterol, HDL-chol, LDL-chol and triglyceride) were of both groups was compared by student 't' test. Levels of total testosterone and free testosterone was presented as percentage (pie chart). P values less than 0.5% was taken as significant.

Results:

Table 1: Demographic characteristics of Hunza group and Punjab group with age above 65 years

Hunza group	Punjab group
BMI (Kg/m^2) 24.55 (90%) 26.18 (10%)	BMI (Kg/m^2) 24.55 (15%) 28.18 (85%)
Social habits Naswar-----65% Smoker-----30% No addiction - 05%	**Social habits** Naswar ---- 05% Smoker ---- 70% No addiction--25%
Chronic illness Diabetes -- 05% Hypertension—07% Tuberculosis-- 20% Any other ---05%	**Chronic illness** Diabetes ---05% Hypertension—07% Tuberculosis - 20% Any other--- 05%
No of children 6-7 ------- (85%} 4-5 -------(15%) No children (0%)	No of children 2-3 (80%) 1-2 (05%) No children (15%)
Reason of no children Male infertility---0% Female infertility---0% Don't know -- 0%	Reason of no children Male infertility---70% Female infertility---20% Don't know -- 10%
Socioeconomic status A—class---(20%) B---class---(60% C---class—(20%)	Socioeconomic status A—class---(25%) B---class---(65% C---class—(10%)
Life style Active -- (85%) Sedentary (15%)	Life style Active---(85%) Sedentary (15)
Dietary Pattern Meditarrian diet or diet containing veg, fruits and meat in proper ratio (90%)	Dietary Pattern Meditarrian diet or diet containing veg, fruits and meat in proper ratio (35%)

Vegetable diet---(10%)	Junk food (50%) Vegetable (15%)

Demographic details showed that people belonging to Hunza Gilgit valley had normal body weight with active life style as compared to people of Punjab . Majority of the Hunza group used naswar as compared to cigarettes, whereas most of people of Punjab group were smokers. Diseases including diabetes, hypertension were more prevalent in Punjab group as compared to Hunza group. Fertility rate was higher in Hunza men who were using mediterranean diet compared to Punjab group (Table 1).

Table 2: Lipid profile of Hunza group and Punjab group

	Hunza group	Punjab group
Serum cholesterol (mg/dl)	140.56±5.61	191.56±38.45**
Serum triglyceride (mg/dl)	135.33±33.34	179.17±41.84**
HDL-cholesterol (mg/dl)	43.17±2.01	38.44±1.76
LDL-cholesterol (mg/dl)	133.59±2.31	154.89±17.82*
Total testosterone (ng/ml)	7.98±1.03	5.91±1.92

**P showed high significant difference
*P showed significant difference

Levels of testosterone is non-signifciantlyhigher in Hunza group compared to Punjab group. However lipid profile including serum cholesterol, triglyceride, HDL-chol and LDL-cholwere significantly higher in Punjab group as compared to Hunza group (Table 2: Fig 1).

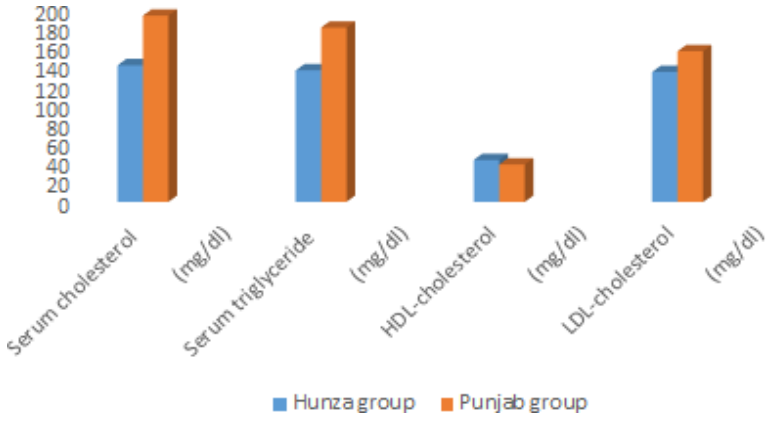

Figure 1: Low levels of lipid profile in Hunza group compared to Punjab group

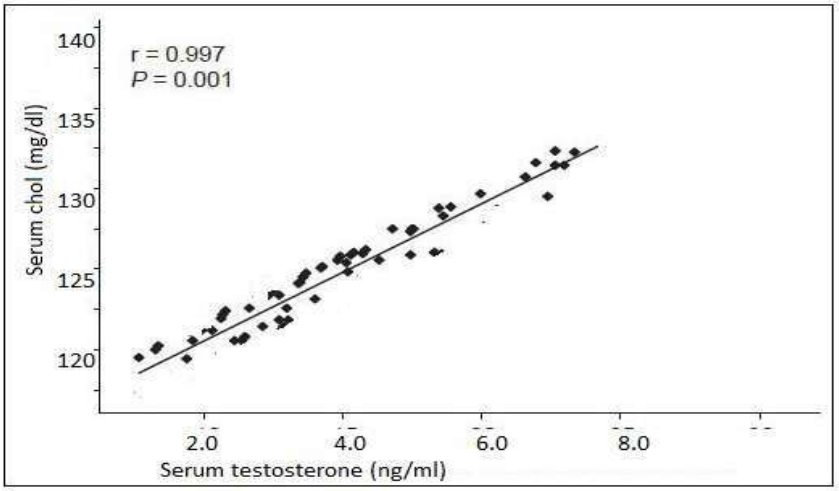

Fig 2: Significant correlation between serum cholesterol and testosterone in Hunza group people

Percentage of total testosterone was non-significantly more in Hunza group versus Punjab group. High levels of testosterone with low values of cholesterol observed in Hunza group (Fig 2)

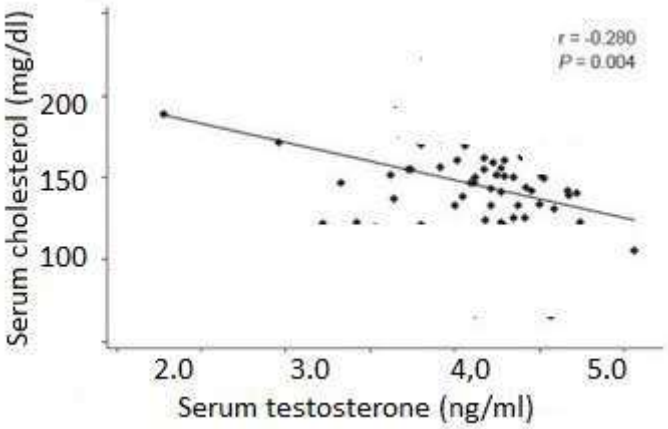

Figure 3: High level of cholesterol with low serum level of testosterone in Punjab group

Low levels of testosterone with high values of cholesterol seen in Punjab group (Fig 3).

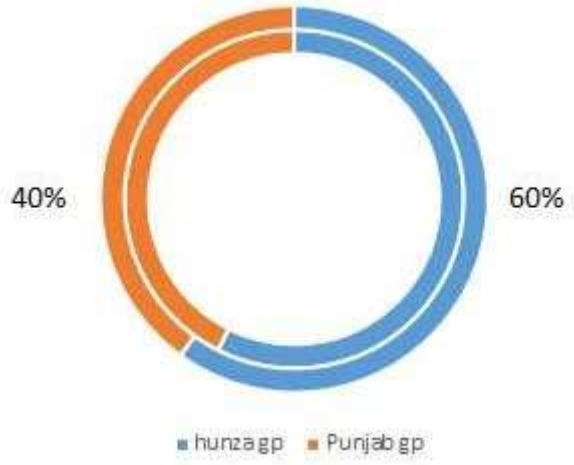

Figure 4 showed percentages of serum testosterone in Hunza group (60%) and Punjab group (40%)

Table :3 showing Testosterone, Melatonin and Prolactin levels and their ratios in Hunza and Punjab men 65 and above.

	Age(yr)	TT ng/dl	Melatonin pg/ml	T/MT ratio	Prolactin ng/ml	T/prl ratio
Hunza(Hilly area)	70	550.4	89.74	6.04	14.84	36.47
Punjab	70	362.93	23.05	18.55	18.51	18.88

	Grouping	N	Mean	Std. Deviation	p-value
Age(yr)	hilly area	57	70	13.131	
	Control	0[a]	.70	.	
TT ng/dl	hilly area	57	550.40	180.802	0.085
	Control	41	362.93	126.854	
Melatoninpg/ml	hilly area	57	89.74	12.836	0.747
	Control	41	23.05	15.987	
t/melatonin ratio	hilly area	57	6.0433	2.33813	0.000
	Control	41	18.5463	7.20056	
Prolactinng/ml	hilly area	57	14.84	2.914	0.000
	Control	41	18.51	5.559	
t/prl ratio	hilly area	57	36.470	9.7348	0.408
	Control	41	18.878	9.1329	

- **Testosterone/Melatonin Ratio** is **much higher** in the **control group**, suggesting that melatonin levels are relatively lower in those individuals compared to their testosterone.

Conversely, the **Testosterone/Prolactin Ratio** is **higher in the hilly area group**, potentially reflecting lower prolactin or higher testosterone, which could indicate better endocrine resilience or reduced stress hormone interference in those environments**.**

Discussion

Lahore, is the last district of Punjab, having a hot humid/non humid climate. In Pakistan, all the research work is mainly based on the population of big urban centers like Lahore, and less than 1% of it is carried out in hilly areas like Gilgit, Skardu,and Hunza. Therefore, it is needed to bring these areas to the limelight, so that research work based ondiet,physical activities,lipid profile and testosterone levels should be carried out to find their correlation with fertility. Very less literature is available related to these parameters in Pakistan or globally[18].

Number of studies were carried out to find the correlation between lipid levels and semen parameters including testosterone, but the results have been inconsistent. Some studies found a positive correlation[19,20]. However, other studies did not find a correlation between the two[21.22]. It is found in different researches that reduced testosterone may impair spermatogenesis, which in turn decreases the number of spermatozoa. Increased and disrupted lipid profile or impaired lipid metabolism can affect the production and secretion of testosterone[23]. Our study showed that serum testosterone levels in hyperlipidemia patients were lower than those of normal men, which was consistent with the findings of some studies[24,25].

A study from Northern Pakistan showed that 15% of the subjects had normal motility and a count of sperm[26]. Our study found 17% of azoospermia while another study from Pakistan reported 13% of azoospermia. Other studies from the European and African countries also reported similar findings[27]. Our study showed infertility cases were more in area of Punjab or plane areas. The reason may be high-temperature and stressing work environment which could have resulted in an abnormal sperm production, motility, and morphology[28,29]. In a European country France, a study was carried out to find the level of fertility in people. Study observed that the people had successful productive life due to cold climate. The subjects were provided warm under garments to be worn for 12-16 hours/ daily for 125 days. After then, Semen analyses wascarried out and level of testosterone was estimated. Decreased rate of spermatogenesis was seen; the results of this study is comparable to our study[30].Number of animal studies have also shown that heat exposure regularly may give anoverwhelming effect on production of sperm production[31,32].

Moreover, in this study we studied Melatonin and Prolactin levels as well which showed surprising results. As most of the people in non-hilly areas are doing jobs and have stressing life styles which tends to decrease their Melatonin which disrupts their sleep and causes problems with their hormonal balance as well.In case of prolactin levels in both Hilly and Non Hilly areas men it is observed that prolactin in Hilly area is less and in non-hillyareas increased levels of prolactin was observed which depicts hyperprolactinemia in non hilly area men showing imbalance in their hypogonadal pituitary axis.

Conclusion

As compared to people living in land area (Lahore, Punjab), high level of testosterone,melatonin with low levels of lipid profile and prolactin was observed in group of people living in hilly areas. Multi-centric researches are required to further explore the relationship of fertility with lipid profile, testosterone,melatonin and prolacti levels and climate /environment in detail to reacha better conclusion. The importance of environmental factors for healthy ageing is increasingly recognized. The consistent implementation of protective means are not yet successful and they need further scientific research. In future we will carry out sexual health of aged males with respect of socioeconomic factors.

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