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1. Title page
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Acknowledgment

No authorship needs to be assigned in order to recognize the contributions of any individual, group, or organization. It's important to be clear about the many kinds of help that will be provided, such as administrative assistance from the department head, technical assistance, monetary funding, and supplies.

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Articles in journals

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Excitotoxicity, a term first coined in the 1960s by Dr. John Olney, represents one of the most paradoxical mechanisms in neuroscience: the same excitatory neurotransmission that sustains life and cognition can, when dysregulated, lead to neuronal death. This phenomenon, marked by excessive stimulation of glutamate receptors—especially NMDA and AMPA receptors—has been implicated in a variety of neurological disorders, ranging from acute insults like stroke and traumatic brain injury to chronic conditions such as Alzheimer’s disease, Parkinson’s disease, and amyotrophic lateral sclerosis (ALS) (1,2).

At the heart of excitotoxicity lies glutamate, the principal excitatory neurotransmitter in the central nervous system (CNS). Under physiological conditions, glutamate binds to ionotropic and metabotropic receptors, modulating synaptic transmission and plasticity. However, during pathological states—such as ischemia or energy failure—extracellular glutamate accumulates due to impaired uptake by astrocytes or uncontrolled release from neurons. This surplus leads to prolonged receptor activation, excessive Ca^{2+} influx, mitochondrial dysfunction, oxidative stress, and ultimately, apoptosis or necrosis (3).

One of the most well-characterized excitotoxic cascades is observed in ischemic stroke. When cerebral blood flow is compromised, ATP depletion impairs ion pumps, leading to neuronal depolarization and massive glutamate release. This uncontrolled excitation results in neuronal swelling, free radical generation, and activation of

Unmasking Excitotoxicity—A Double-Edged Sword in Neurodegeneration

degradative enzymes—all hallmarks of excitotoxic injury (4).

Despite the well-established role of excitotoxicity in disease pathophysiology, translating this knowledge into effective clinical interventions has proven difficult. Numerous glutamate receptor antagonists have failed in clinical trials due to issues of toxicity or limited efficacy. For instance, NMDA antagonists like memantine have shown modest benefits in Alzheimer’s disease, but broader application has been constrained by neuropsychiatric side effects (5).

Nevertheless, recent advances offer renewed hope. Targeting downstream signaling pathways, enhancing glutamate uptake through astrocytic transporters, and modulating receptor subtypes more selectively are emerging strategies. Furthermore, the role of glial cells and neuroinflammation in modulating excitotoxicity has gained attention, suggesting that a more holistic view of the neurovascular unit may be necessary to devise successful therapies (6).

Excitotoxicity remains a compelling illustration of how a fundamental physiological process, when misregulated, becomes pathogenic. Continued research is essential to unravel its complexity and to design targeted interventions that preserve neuronal integrity without compromising essential synaptic function.

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Use of Anxiolytic with Antihypertensive
Drugs in a Tertiary Care Hospital

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Abstract

Objectives: The present study was conducted to see the use of prescribing pattern of anxiolytic with antihypertensive drugs in a tertiary hospital. **Methods:** It was an observational type of cross sectional study. The study was performed among hypertensive patients (both indoor and outdoor) of Cardiology department in MMCH who received antihypertensive drugs. **Results:** Out of 400 hypertensive patients 67% were male and 33% were female. Mean age of the patients was 55.02 ± 12.47 years. Systolic BP was 146.74 ± 28.28 and diastolic BP was 90.60 ± 14.27 and the highest percentage of patient were found in Stage 2 HTN (50.25%) according to JNC-7 guidelines. In our study 5 groups of antihypertensive were prescribed (ARB, ACEI, BB, Diuretics, and CCB). It was found in this study that out of 400 prescription anxiolytic used in 242 prescription that was 60.50%. **Conclusion :** Clonazepam was the most commonly used anxiolytic that was 186 (76.90%) and 2nd most common anxiolytic was Bromazepam 50 (20.70%).

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Keywords: Antihypertensive drugs, anxiolytic

Introduction

Maduram 2013 conducted a study on prescription pattern of antihypertensive drugs in Shrisathyasai Medical College & research institute and described high blood pressure, termed "hypertension," is a condition that afflicts almost 1 billion people worldwide and is a leading cause of morbidity and mortality. Therefore, this disease is sometimes called the "silent killer." This disease is usually asymptomatic until the damaging effects of hypertension (such as stroke, myocardial infarction, renal dysfunction, visual problems, etc.) are observed. Hypertension is a major risk factor for coronary artery disease, myocardial infarction ("heart attacks") and stroke.(1)

From the estimated prevalence of hypertension would increase from 26.4% in 2000 to 29.2% in 2025. Hypertension (HTN) is one of the major chronic diseases resulting in high morbidity and mortality in the world population. Prevalence of HTN in India is reported to vary from 4-15% in urban and 2-8% in rural population. Socioeconomic, behavioral, stressful lifestyle and nutritional issues of the people led to enormous increase of cardiovascular diseases. HTN and Diabetes Mellitus (DM) frequently coexist which increases with age. HTN is about twice as common in patients with DM as in those without (8%). More specifically, it has been reported that individuals with blood pressure values of 130-139/85-89 mmHg were significantly in higher risk of developing cardiovascular diseases compared to subjects with lower blood pressure (2).

Report 2002 of the World Health Organization (WHO) states that high blood pressure is the primary or secondary cause of 50% of all cardiovascular diseases worldwide. Hypertension is an important risk factor for cardiovascular accidents, coronary heart disease and cardiac hypertrophy with heart failure, aortic dissection, and renal failure. The worldwide burden of hypertension in 2000 was estimated to be 972 million or 26.4% of the adult world population, with 333 million in economically developed and 639 million in economically devel-

oping countries. It has been estimated that by 2025, 1.56 billion individuals will have hypertension; an increase of 60% from 2000. Most of this rise can be attributed to an expected increase in the number of people with hypertension in economically developing countries (3).

Therefore, the prevention, detection, treatment and control of this condition demand high priority (3). Management of hypertension is an important step to decrease the mortality and morbidity of cardiovascular disease and to prevent uncontrolled complications (4).

It is well understood that emotional reactivity and anxiety is associated with increased risk of hypertension where support management of anxiety is crucial in hypertensive patient (the role of anxiolytics in hypertensive urgency management) (5). Anti-anxiety treatment is effective in lowering BP in patients with excessive hypertension. Thus, anxiolytic treatment may be considered in patients with excessive hypertension without acute target organ damage (6).

Materials and Methods

This study was a record based observational type of descriptive cross-sectional study was conducted for a period of 6 months from July 2015 to December 2015 in Cardiology department of Mymensingh Medical College Hospital, Mymensingh. 400 patient were collected from both indoor and outdoor. This study includes hospital In-patients and Out-patients with hypertension with or without IHD and DM treated for hypertension at Cardiology department. The inclusion criteria were: Patient with the age group ≥ 18 years, hypertension with or without ischemic heart disease, hypertension with or without DM. Exclusion criteria were: patients with disease like hepatic disease and pregnancy. Non-Random sampling was employed for

collecting data. The entire relevant data were analyzed with the aid of Statistical Package for Social Sciences (SPSS) version 21 software to generate descriptive statistics. The data collected was analyzed with frequency, simple percentage, mean and standard deviation. The results presented in texts, tables and figures.

Observations and Results

Out of 400 patients, 268 (67%) were male and 132 (33%) were female. So, male were found more than their female counterparts.

Table 1: Demographic Characteristics (age) of Patient

Demographic Characteristics	Male	Female	Total
Mean age (years)	56.45	52.12	55.02
Standard deviation	12.20	12.58	12.47
Minimum age (years)	20	25	20
Maximum age (years)	90	90	90

Table 6.20: Frequency of using anxiolytic with antihypertensive

Use of anxiolytic	Frequency	Percentage
Used	242	60.50
Not used	158	39.50
Total	400	100

Table 6.21: Pattern of using anxiolytic

Name of anxiolytic	Frequency	Percentage
Clonazepam	186	76.9
Bromazepam	50	20.70
Alprazolam	04	1.65
Diazepam	01	0.41
Clobazam	01	0.41
Total	242	100

Observations and Results

Table 6.20 & 6.21 show that out of 400 prescription anxiolytic used in 242 prescription that was 60.50%. Clonazepam was the most commonly used anxiolytic that was 186 (76.90%). Other anxiolytic prescribed in our study were Bromazepam, Alprazolam, Diazepam, Clobazam and their no. & percentage in our study were 50 (20.70%), 04 (1.65%), 01 (0.41%), 01 (0.41%) respectively. All of them belongs to Benzodiazepine group.

Discussion

The study was conducted during the period of July 2015 to June 2016 in the department of Cardiology, Mymensingh Medical College Hospital, Mymensingh to evaluate the use of anxiolytic with antihypertensive in hypertension with or without ischemic heart disease and DM at Cardiology Department. It was an observational type of descriptive cross sectional study.

In this study the prevalence of hypertension was seen more in male (67%) than their female counterparts (33%) which corresponds to the findings of other studies Joseph S, Varghese N & Thomas L (3), Konwar M, Paul PK & Das S (7) and Rachana PR, Anuradha HV & Shivamurthy MC (8).

In our study mean age of the patients was 55.02 ± 12.47 years. A study in New Delhi, India done by Sharma AK, Dahiya N, and Kairi JK et al. and found the mean age of the patients was 58.25 years which was similar to this study (9). Another study conducted by Madhwar A, Gupta D, and Singh S et al. (10) and found the mean age of the patients was 58.9 ± 11.9 years which was also similar to the present study.

It was found in this study that out of 400 prescription anxiolytic used in 242 prescription that was 60.50%. Clonazepam was the most commonly used anxiolytic that was 186 (76.90%) and 2nd most common anxiolytic was Bromazepam 50 (20.70%). Muhit et al. (2012) conducted a study in Bangladesh and described the physician's prescribed anxiolytic drugs for 81.41% cases and most common anxiolytic drugs reported in their study was benzodiazepine groups. Bromazepam (62.52) was preferred by most of the physicians. Clonazepam (24.72%) and diazepam (10.39%) were also prescribed to the patients which was dissimilar to this study (11).

Paštrović F et al conducted a study in Croatia & found majority of Patient with hypertension received benzodiazepine group of anxiolytic drugs (12). Grossman E et al. conducted a study about antianxiety treatment in patients with excessive hypertension & found antianxiety treatment is effective in lowering BP in patients with excessive hypertension (6).

Conclusion

Hypertension is a chronic incurable disease. Maintaining the control of blood pressure is very important in HTN. From our study it was concluded that HTN is more prevalent in male than female & Mean age of the patients was 55.02 ± 12.47 years out of 400 prescription anxiolytic used in 242 prescription that was 60.50%. Clonazepam was the most commonly used anxiolytic that was 186 (76.90%). Thus,

anxiolytic treatment may be considered in patients with hypertension without acute target organ damage. Further large placebo controlled studies are required to prove the benefit of anxiolytic agents.

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Comparison of TSH between Combined Oral Contraceptive Pill Users and Non-user Women: A Cross-sectional Study

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Abstract

Background: Normal thyroid function is mandatory for healthy life. Normally there is a fine balance between the free and bound thyroxine in the body that can be altered by combined oral contraceptive pill which contain estrogen and progesterone. And this alteration is clearly assessed by thyroid stimulating hormone (TSH). **Objectives:** The aim of this study was to estimate and compare the thyroid-stimulating hormone (TSH) among the oral contraceptive pill users and non-user women in Rajshahi City. **Methods:** This cross-sectional comparative study was carried out from January 2022 to December 2022 in the Department of Physiology, Rajshahi Medical College, Rajshahi. The study was conducted on 120 married women aged 18-40 years. Among them 60 women were combined oral contraceptive pill users and 60 women were COCP non-users. TSH parameter was estimated using the auto analyzer machine. Data were analyzed by SPSS software, version 24 and p value < 0.05 was considered statistically significant for all tests. **Results:** The mean age of COCP user women was 30.22 ± 7.30 years and the COCP non-user women was 32.63 ± 7.81 years. COCP user women with mean BMI 26.57 ± 2.94 kg/m² compared with COCP non-users with BMI of 24.54 ± 2.67 kg/m². The mean TSH value in COCP user women was found 1.92 ± 0.83 μ IU/ml and in COCP non-user women was 1.50 ± 0.76 μ IU/ml and it was statistically significant ($p < 0.01$). **Conclusion:** The present study had showed an increased level of TSH in combined oral contraceptive pill user women group than COCP non-users group. Present study findings indicated the tendency to develop subclinical hypothyroidism among COCP users. Routine monitoring of thyroid function status is a time demanding issue as widespread use of combined oral contraceptive now-a-days. Early detection of hypothyroidism might reduce complications and give women a healthy life.

Keywords: Combined oral contraceptive pill, Thyroid stimulating hormone.

Introduction

In 2022, Bangladesh was the eighth most populous country in the world, with an estimated population of 167 million. Bangladeshi population is equivalent to 2.11% of the total world population. The country's population density, roughly 1,265 people per square kilometer, is also one of the highest in the world (1). About 40% of the total population is under the age of 15 and about 50% of the population is within reproductive age. Bangladesh cannot achieve sustainable development without continued efforts to curb population growth. It is a positive issue that choice of contraceptive methods has considerably increased over recent years in Bangladesh. Now contraceptive prevalence rate (CPR) is 62% that was only 8% in 1975 (2). Oral pill is the most widely used (27%) method, followed by injectables (12.4%), condoms (6.4%), female sterilization (4.6%), male sterilization (1.2%), implants (1.7%) and IUDs (0.6%) (2). As the most common form of effective and reversible contraception, the prevalence of use of birth control pills among women aged 15–45 is 17% and 27.3% among all methods of contraception in the Bangladesh (2). Moreover, use of birth control pills declined as age increased: 54% of users of contraceptives are under 20 years old, 35% are 20–40 years old and only 11% are 40–45 years old (3).

Among birth control pill combined oral contraceptive pill (OCP) is commonly used in Bangladesh due to free Government supply named as Sukhi from community clinic to tertiary level hospital. It was first designed to inhibit ovulation and thus used for birth control (4). Over time, combined OCP is used not only for prevention of unwanted pregnancies but also as treatment for abnormal uterine bleeding, endometriosis, menstrual and hormonal disorders etc. Additionally, long-term use of combined OCP (≥ 10 years) could significantly decrease the risk of ovarian and endometrial cancer (5).

However, COCP can also bring many adverse effects including increased risk of hypertension, thromboembolic events, breast cancer, serious

autoimmune diseases and especially endocrine related dysfunctions (6,7). Among endocrine dysfunctions, thyroid disorders are important. The thyroid gland produces hormones—predominantly the prohormone T4 and a small amount of the bioactive hormone T3 that play a role in normal growth, energy metabolism and reproduction (8,9). Most T3 is produced by deiodination of T4 in peripheral tissues through the action of deiodinases. Thyroid secretion is controlled primarily by thyroid stimulating hormone (TSH) secreted by anterior pituitary gland. The effects of thyroid hormones depend on the amount of hormone that reaches the tissues, their activation and the availability of specific hormone receptors in the nucleus and cytoplasm of the cells. Under normal conditions, the levels of free thyroid hormones are adjusted by appropriate stimulation or suppression of hormone secretion and elimination mechanisms. The total serum concentration is usually maintained at a level proportional to the thyroid-binding globulin (TBG) concentration and appropriate to maintain a constant level of the free form of the hormone (10,11). In combined oral contraceptive pill, there are two components oestrogen and progesterone. The proportions of these two components vary based on formulation time to time. The oestrogenic component of the OCP is capable of increasing various liver proteins such as thyroid binding globulin (TBG), sex hormone-binding protein (SHBG) and coagulation factors. As a result, increased TBG alter the delicate balance of free and bound thyroid hormone in our body because free T4 is bound to the increased TBG and there is less free T4 in our body for performing function. TBG has more affinity to T4 than T3 and represents over 70% of the total hormone bound to proteins (12). On the other hand, the role of progesterone is to modulate oestrogen-dependent effects mainly through their anti-androgenic action. As both progesterone and thyroid are members of the steroid hormone superfamily, they compete each other for binding with the receptors of steroid (13).

Therefore, in short time use of combined oral contraceptive pill, individuals develop subclinical

hypothyroidism and longtime use of combined OCP individuals develop hypothyroidism. Hypothyroidism refers to the common pathological condition of thyroid hormone deficiency. If untreated, it can lead to serious adverse health effects and ultimately death. Because of the large variation in clinical presentation and general absence of symptom specificity, the determination of hypothyroidism is pre-dominantly biochemical. Clinical manifestations of hypothyroidism range from no signs or symptoms to life threatening (14). Despite these plausible hypothetical relationships between the physiologies of the thyroid axis and combined oral contraceptive pill, there were few studies of thyroid function in relationship to exogenous oestrogen and progesterone. In Bangladesh, there were few studies regarding relationship between the thyroid function and combined oral contraceptive pill use. Therefore, this study might be useful to generate new data on effect of combined oral contraceptive pill on TSH in our population.....

Materials and Methods

This cross-sectional type of comparative study was conducted in the Department of Physiology, Rajshahi Medical College, Rajshahi from January 2022 to December 2022 to find out the association between combined oral contraceptive pill use and thyroid stimulating hormone level among the married women in Rajshahi City. The study population was married women aged 18 to 40 years in Rajshahi city. A purposive sampling technique was used and the final sample size was 120. 60 women aged 18 to 40 years under combined OCP were included in one group and similar numbers of women aged 18 to 40 years without under combined OCP were included in another group purposively. The selection was from neighbours, relatives and staff who were resident of Rajshahi and women who were attend in Maternity and Child Welfare Centre

of Rajshahi for services. Consulting with the guide and reviewing the previous published literature, the questionnaire was developed for the study. Prior to data collection, respondents were briefed about the purpose of the study and their informed written consent was taken. After taking informed written consent, complete history taking and physical examination were done and recorded in preformed data sheet. Then blood sample was obtained from median cubital vein in antecubital fossa making the subject to sit comfortably in a chair. Through a sterile DISPOVAN syringe under sterile precautions, about five milliliters of blood was collected in EDTA coated vacutainers. The sample was then analyzed for the TSH parameter by using auto-analyzing machine.

Results

The mean age of the COCP user women was 30.22 ± 7.30 years and the COCP non-user women was 32.63 ± 7.81 years (Table-01).

Table 1: Distribution of the respondents according to age (n=60 in each group).

Age in years	COCP user women	COCP non-user women
	Frequency (%)	
< 25 years	14 (23.30)	14 (23.30)
25-35 years	30 (50.00)	21 (35.00)
> 35 years	16 (26.70)	25 (41.70)
Total	60 (100.00)	60 (100.00)

$\bar{X} \pm SD = 30.22 \pm 7.30$ years, range = (18 – 42) years in COCP user women.

$\bar{X} \pm SD = 32.63 \pm 7.81$ years, range = (18 – 42) years in COCP non-user women.

The occupational status of the women revealed that among the COCP user women, majority (76.70%) of the respondents were housewife, 18.30% were NGO worker and only 5% were Govt. service holder. Similarly, in the COCP non-users group, majority (75%) of the women were housewife, 13.30% were NGO worker and remaining 11.70% were Govt. service holder. In both groups, housewife respondents were proportionately higher (Figure-I).

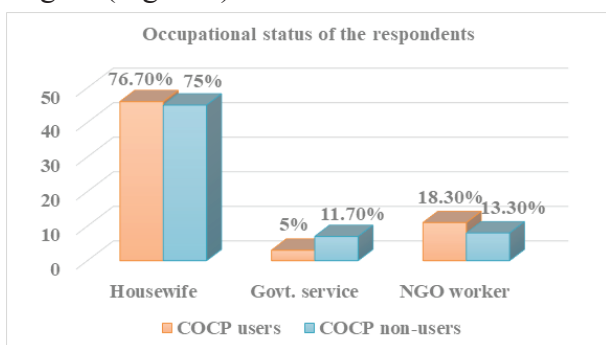


Fig I. Distribution of the respondents on the basis of occupational status (n=60 in each group).

The mean BMI of the COCP user women was $26.57 \pm 2.94 \text{ kg/m}^2$ and the COCP non-user women was $24.54 \pm 2.67 \text{ kg/m}^2$ (table-02).

Table 2: Distribution of individuals with a single abnormal lipid parameter (n=80)

BMI (kg/m ²)	COCP user women (n=60)	COCP non-user women (n=60)
	Frequency (%)	
Underweight (< 18.5)	0 (0.00)	4 (6.70)
Normal (18.5 to 24.9)	21 (35.00)	27 (45.00)
Overweight (25 to 29.9)	30 (50.00)	29 (48.30)
Obese (30 to 39.9)	9 (15.00)	0 (0.00)
Total	60 (100.00)	60 (100.00)

$\bar{X} \pm SD = 26.57 \pm 2.94 \text{ kg/m}^2$ in COCP user women.
 $\bar{X} \pm SD = 24.54 \pm 2.67 \text{ kg/m}^2$ in COCP non-user women.

In COCP users group, 100% of the women had normal TSH and in the COCP non-users group, most (96.70%) of the women had normal and only 3.3% had low level of TSH (Table-03).

Table-03: Estimation of TSH in COCP users and non-user women (n=60 in each group).

Parameter	Group	Below the normal ranges	Normal ranges	Above the normal ranges
		Frequency (%)		
TSH	COCP users	0 (0)	60 (100)	0 (0)
	COCP non-users	2 (3.3)	58 (96.70)	0 (0)

TSH level in COCP user women was higher than the COCP non-user women and it was statistically significant ($p < 0.01$) (Table-04).

Table-04: Comparison of TSH level between COCP users and non-user women (n=60 in each group).

Group	TSH ($\mu\text{IU/ml}$)		t-value	p-value
	mean \pm SD	Range		
COCP user women	1.92 \pm 0.83	0.88 to 4.20	2.90	< 0.01
COCP non-user women	1.50 \pm 0.76	0.09 to 3.50		

(Data were analyzed by **Unpaired t-Test** and were presented as **mean \pm SD**. p value < 0.05 was considered as significant.)

There was statistically significant positive correlation between serum TSH level and duration of COCP use among pill user women ($p < 0.001$) (Figure-II).

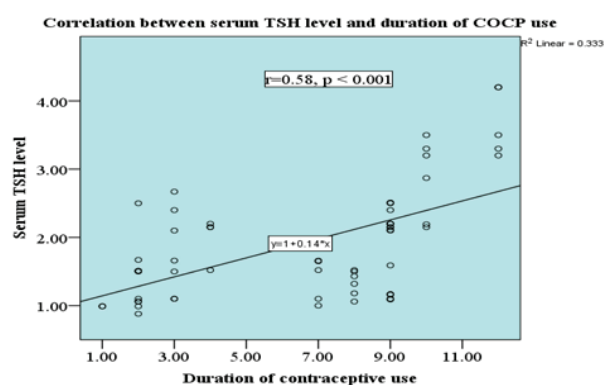


Fig II. Scatter diagram showing correlation between serum TSH level and duration of COCP use (n=60).

Discussion

The use of hormonal contraceptives is more common and has exponentially increased day by day. No substance used is without side effects, that is why it is necessary to know the possible side effects of combined oral contraceptive pill. Due to use of combined oral contraceptive pill that contain both estrogen and progesterone can alter that delicate balance of free and bound thyroid hormone in the body. The estrogen in birth control pills increases the amount of thyroid binding proteins that is available for binding of thyroid hormone. So, there is less functioning thyroid hormones in the body.

In the current study, among COCP users group, 50% of the respondents were overweight, 35% had BMI within the normal range and 15% were obese. On the other hand, in the COCP non-users group, 48.30% of the women were overweight, 45% women had BMI within the normal range and only 6.70% were underweight. The mean BMI of the COCP user women was $26.57 \pm 2.94 \text{ kg/m}^2$ and the COCP non-user women was $24.54 \pm 2.67 \text{ kg/m}^2$. These findings were not similar with a study done by Qiu et al (15). where in pill users group 35.90% had BMI within the normal range, 31.30% were obese, 28.40% were overweight and 4.40% were

underweight. On the other hand, 40.30% of pill non-user women were obese, 28.80% were both overweight and normal weight and 2.10% were underweight. These dissimilarities might be due to food habit and life style varies in different geographical areas.

In the current study, serum TSH in COCP user women was $1.92 \pm 0.83 \text{ } \mu\text{IU/ml}$ and in non-user women was $1.50 \pm 0.76 \text{ } \mu\text{IU/ml}$ and it was statistically highly significant ($p < 0.01$). Similar findings were also found in a study that was done by Knudsen et al (16). in Denmark where serum TSH was 1.24 mU/l in non-users of oral contraceptive pill and 1.35 mU/l in users of pill and it was statistically significant ($p < 0.01$). Berair and Abdalla (17) in Sudan reported that TSH level in pill user women was $6.40 \pm 1.46 \text{ mIU/L}$ and in pill non-user women was $1.88 \pm 0.87 \text{ mIU/L}$ and it was statistically significant ($p < 0.05$) which findings were also in accordance with our study findings. Similar findings also found with the studies done by Weeke and Hansen (18), Kuhl et al. (19), Rumsey et al. (20), Zaninovich et al. (21) and Muller et al. (22). But findings were not similar with a study done by Al-Youzbaki and Mahmood (23) in Iraq where free TSH level in COCP user women was $1.74 \pm 0.94 \text{ Pmol/L}$ and in COCP non-user women was $1.71 \pm 0.82 \text{ pmol/L}$ and it was statistically non-significant ($p > 0.05$). High blood levels of estrogen signal the liver to increase the production of thyroid-binding globulin (TBG). This is an inhibitor protein that binds to the thyroid hormone, reducing the amount of free T3 and free T4 available for use by cells. In response, thyroid gland cranks up production of TSH to compensate for the deficit.

Contradictory findings were also found in the studies done by Duijkers et al. (24), Khalil (25) and Wiegratz et al. (26) where there were no statistically significant different of serum TSH level between COCP pill users and non-user women. Study to study

dissimilarities might be due to duration of contraceptive use which was not same among the women.

In this study, there was statistically significant positive correlation between serum TSH level and duration of COCP use among pill user women ($p < 0.001$). These findings were in accordance with a study done by Al-Youzbaki and Mahmood (23). But contradictory findings were found in a study done by Berair and Abdalla (17) where there was statistically non-significant positive correlation between serum TSH level and duration of COCP use. In the current study there was statistically non-significant positive correlation of total T3 & T4 level with duration of COCP use among pill user women ($p > 0.05$). Similar findings were found in a study done by Berair and Abdalla (17).

In the present study, OCP users showed non-significantly lower FT4, FT3 but significantly higher TSH level than the non-OCP users. It indicates a tendency to develop subclinical hypothyroidism among the OCP users. Consequently, regular screening of thyroid function is necessary among the OCP users.

So, the use of oral contraceptives is a predictor for variation in thyroid hormone concentrations due to estrogen mediated TBG-induced hepatic synthesis which is clearly understood by measuring TSH level. The use of contraceptives should be considered in diagnostic evaluation of thyroid diseases owing to their capacity to modulate the limits of thyroid hormone distinct reference intervals.

Conclusion

Present study concluded that long term OCP intake causes increased TSH level among the COCP users which is an indicator of a tendency to develop subclinical and clinical hypothyroidism.

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Morphometric study of the vertebral body in fully ossified dry human fifth lumbar vertebrae.

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Abstract

Background: Knowing the exact vertebral body size is an important factor in diagnosing and treating spinal deformation. For successful surgery and suitable instrumental design, adequate anatomical knowledge of the lumbar vertebra is needed. The present study was carried out to create a morphometric database of the bodies of the fifth lumbar vertebrae. **Material and Methods:** A cross-sectional, analytical type of study was conducted in the Department of Anatomy, Dhaka Medical College, Dhaka from January 2022 to December 2022. Measurement of superior and inferior body length was done using a digital Vernier caliper. **Results:** The mean (\pm SD) of the superior and inferior body length was higher in males than females and showed a statistically significant difference ($p < 0.001$). **Conclusion:** All the measured values of different variables of the fifth lumbar vertebra were greater in males than females. The current data should be considered during spinal surgery to avoid any complications that might result from the mispositioning of spinal implants.

Keywords: Superior vertebral body length, Inferior vertebral body length

Introduction

Despite the massive size of the fifth lumbar vertebra, the vertebral bodies experience tremendous loading stress due to the loads raised and transported by the upper extremities (1). Lumbar vertebral fractures are a common occurrence in osteoporosis. The vertebral body can develop any benign bone tumor, including chondroma, osteoma, fibroma, hemangioma, etc. The most frequent cancers to spread to the vertebrae are those of the breast, lung, prostate, kidney, gastrointestinal tract, and thyroid (2). For a variety of spinal conditions, including lumbar fractures, removal of tumors in vertebral bodies, gross spondylolisthesis, and lumbar instabilities, the lumbar spine must be fixed (3). Many devices, such as rods, plates, and wires can be placed on the spine for fixation or immobilization with the use of a screw. Most spine disorders can be directly accessed through the anterior approach through the vertebral body, which also permits ideal neural decompression, sufficient realignment, and robust reconstruction or fixation. To avoid difficulties following the anterior approach, morphometric analysis of the body of the fifth lumbar vertebra is crucial (4). This research is also crucial for selecting the right interbody device, like an artificial disc or inter-body cage, or for bone graft material for inter-body fusion (5). To facilitate diagnosis, treatment planning, and the development of novel surgical procedures in orthopedic and neurosurgery, this study establishes gender- and ethnicity-specific metric criteria for the body of the fifth lumbar vertebra.

Materials and Methods

This cross-sectional study was carried out to construct data on different dimensions of the body of fully ossified dry human fifth lumbar

vertebrae in the Department of Anatomy, Dhaka Medical College. It was ensured that all selected vertebrae were normal, and fully ossified without any congenital or degenerative. Linear measurements of Superior vertebral body length and inferior vertebral body length were done by Digital Vernier Caliper.

To measure the superior body length of the fifth lumbar vertebra, one dot was placed at the anterior aspect of the upper border of the vertebral body at the midsagittal plane marked by A, and another dot was placed at the posterior aspect of the upper border of the vertebral body marked by B. Then the fixed jaw of Vernier caliper was placed on marked point A and the sliding jaw was adjusted to meet the marked point B. The distance between A and B on the superior surface was taken as the superior body length of the fifth lumbar vertebra which was measured by the digital Vernier caliper in millimeters.

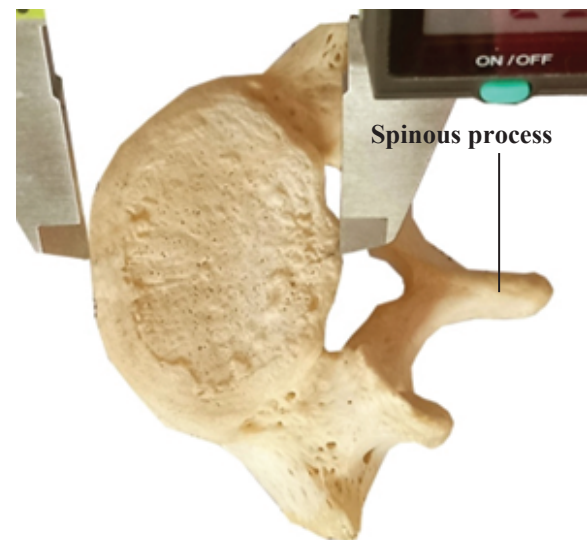


Figure I: Photograph showing the AB line which represents the superior body length of the fifth lumbar vertebra (Superior view)

To measure the inferior body length of the fifth lumbar vertebra another dot was placed at the anterior aspect of the lower border of the vertebral body at the midsagittal plane marked by A and another dot was placed at the posterior aspect of the lower border of the vertebral body at midsagittal plane marked by B. Then the fixed jaw of Vernier caliper was placed on marked point A and the sliding jaw was adjusted to meet the marked point B. The distance between A and B on the inferior surface was taken as the inferior body length of the fifth lumbar vertebra which was measured by the digital Vernier caliper in millimeter.



Figure II: Photograph showing the AB line which represents the inferior body length of the fifth lumbar vertebra (Inferior view)

Ethical Clearance

The study was carried out after approval of the Research Review Committee (RRC) and Ethical Review Committee (ERC) of Dhaka Medical College, Dhaka.

Data Processing And Analysis

The data collected from morphological studies were processed to get mean values and stan-

dard deviations as applicable. The statistical analysis was done by unpaired Student’s t-test for comparison between variables between males and females by using computer-based software, Statistical Package for Social Science (SPSS) version 26.0. Statistical analysis was accepted at a p-value equivalent to or less than 0.05 ($p < 0.05$).

Results

The result is shown in Tables I and Figure 3.

The mean \pm SD of superior and inferior body length in males was 31.95 ± 2.06 mm and 31.22 ± 1.97 mm and in females was 29.87 ± 2.07 mm and 29.33 ± 1.89 mm respectively. The range of superior and inferior body length in males was 26.14 mm to 36.70 mm and 25.84 mm to 36.43 mm and in females was 25.47 mm to 34.77 mm and 25.70 mm to 34.16 mm respectively. The mean superior and inferior body length of the fifth lumbar vertebra was found to be higher in males than in females and the difference was statistically significant ($p < 0.001$).

Table I: Superior and inferior body length of fifth lumbar vertebra in male and female (N = 140)

in mm	Sex		p-value
	Male (n= 76) (Mean \pm SD)	Female (n=64) (Mean \pm SD)	
Superior body length	31.95 ± 2.06 (26.14 – 36.70)	29.87 ± 2.07 (25.47 – 34.20)	.000*
Inferior body length	31.22 ± 1.97 (25.84 – 36.43)	29.33 ± 1.89 (25.70 – 34.16)	.000*

Values in parentheses indicate range values. Comparison of values between males and females was done by Unpaired Student’s ‘t’ test.

* = Significant at $p < .001$

n = Sample size in each group

N = Total number of samples

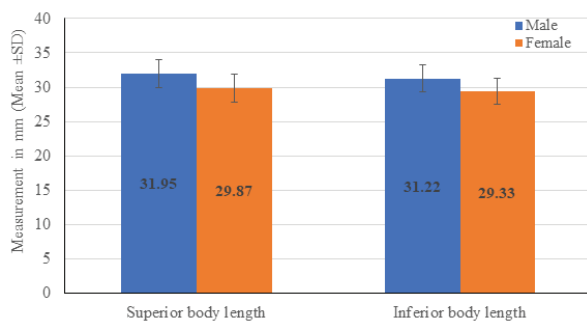


Figure III: Bar diagram showing superior and inferior body length of fifth lumbar vertebra in male and female.

Discussion

It is well established that the morphometric data varies within different sex, race, ethnic, and regional groups (6,7). Population-based normal variations of vertebral body diameters of the fifth lumbar vertebra in the Bangladeshi population are not well documented in the literature. Hence there is a need for our metrical data. The results of the current study were compared with the results of different researchers abroad. Observed results of morphological parameters of the present study showed some similarities as well as dissimilarities with the available data present in different publications.

The mean \pm SD superior body length of the fifth lumbar vertebra in this study in males and females was 31.95 ± 2.06 mm and 29.87 ± 2.07 mm respectively. The superior body length of the fifth lumbar vertebra was greater in males than in females and it was found statistically significant ($p=0.000$). The measured values of the present study were almost like the findings found by Das, et al. (3) (2021, pp.23-29) who conducted a study on the North Indian population and reported that the mean superior body length of the fifth lumbar vertebra was 29.23 ± 4.89 mm. The similarity might be due to similar race and geographical area. According to Azu, et al. (8) (2016, pp.1345-51) conducted a study on the South

African population and recorded that the mean superior body length of the fifth lumbar vertebra was 36.08 ± 4.40 mm and 35.16 ± 2.16 mm in males and females respectively. However, the values of the mean superior body length of the fifth lumbar vertebra were higher than in the present study. The dissimilarity might be due to variations in race.

The mean \pm SD inferior body length of the fifth lumbar vertebra in this study in males and females was 31.22 ± 1.97 mm and 29.45 ± 1.91 mm respectively. The inferior body length of the fifth lumbar vertebra was greater in males than in females and it was found statistically significant ($p=0.000$). Londhe and Garud (9) (2020, pp.77-80) carried out a study on the Indian population and reported that the mean inferior body length of the fifth lumbar vertebra was 29.8 ± 3.3 mm. The mean values of inferior body length were almost like the present study. The similarity might be due to the same race and geographical area. The measured values of the present study were found dissimilar to the findings reported by Alam, et al. (10) (2014, p.421) who conducted a study on the Pakistani population and reported that the mean inferior body length was 33.03 mm and 31.91 mm in male and female respectively. The dissimilarity might be due to multifactorial etiological factors like environment, genetics, geography, and nutrition.

Conclusion

The present study attempted to provide morphometric baseline data of the vertebral body of the fifth lumbar vertebrae which will serve as a normative reference. Knowing the exact vertebral size and shape is an important factor in diagnosing and treating spinal deformation. For successful surgery and suitable instrumental design, adequate anatomical knowledge of the lumbar vertebra is needed. The current data should be considered during spinal surgery to avoid any complications that might

result from the mispositioning of spinal implants. For genuine use, further progressive study in the same direction with a larger sample size from a skeletal collection with known age, sex, stature, and ethnicity is desirable.

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Hypertension Among Elderly Group of Urban Population

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Abstract

Background: Management of hypertension of elderly population is more challenging and complicated. Moreover, hypertension can predispose to many other health issues and disablements which can make this delicate and vulnerable period of life even more strenuous. This study tried to evaluate the prevalence of hypertension among elderly from an urban setting. **Materials and Methods:** This is a cross-sectional type of study conducted during the period of January to December, 2019 among 105 elderly people (≥ 60 years) in a selected area of Mohammadpur Thana of Dhaka district. Data regarding their sociodemographic background, modifiable risk factors for hypertension and hypertensive profile have been assessed and recorded. Ethical approval from the designated authority and informed written consent from the respondents have been collected prior to the commencement of the data collection. **Results:** This cross-sectional study observed 105 respondents aged over 60 years among which 44 (41.90%) respondents were male and 61 (58.1%) respondents were female. Educational status, occupational status, BMI and exercising were the key variables that were found to have a significant relationship with hypertensive status of the respondents ($p < 0.05$). **Conclusion:** With the increase of the educational attainment, not being occupied, being obese and overweight and not doing exercise regularly found to have higher prevalence of hypertension. To evaluate the role of these factors to cause hypertension further longitudinal studies are recommended on national level.

Keywords: Endoscopy guided biopsy, histopathology.

Introduction

Hypertension is a significant cause of morbidity and mortality linked with cardiovascular diseases, which often remains asymptomatic and due its chronic nature it mandates strict regulation of the blood pressure as well as insistent coherence to the medical interventions to prevent consequences associated with this condition (1). Hypertension associated mortality stated to be at 7.5 million annually, which accounts for 12.8% of the total deaths, which also attributes to 57 million disability adjusted life years (DALYS), which accounts for 3.7% of the total DALYS (2). Nearly 45% of global mortality due to heart disease and 51% of deaths due to stroke are prevalent among hypertensive patients (3). Prevalence of hypertension and its associated complications increase with age (4). Increase in life expectancy attributed by better health care provision is causing the elderly group of population to be very rapidly growing (5). As estimated by World Health Organization, amid of 2015 and 2050, world population aged over 60 years will increase by nearly two folds from 12% to 22% (6). Thus it can be anticipated that, high blood pressure and associated co-morbidities are also going to more prevalent among the aging population, which is going to pose a great healthcare challenge. Additionally, modernization and industrialization precipitated a lifestyle with lack of physical activity, unhealthful eating pattern, tobacco use, that raised the prevalence of non-communicable diseases among the elderlies (7). Aging associated hypertension is hypothesized to be attributed by arterial stiffness caused by structural and functional changes in the vessels (8). However, hypertension and its associated baneful consequences are preventable even in old age with the modification of lifestyle and through timely and adequate interventions (4). The condition often remains undetected even when it has advanced to an

aggressive stage (9). Thus, the routine evaluation of an elderly is critical for the early diagnosis, control of high blood pressure and providing with adequate treatment (10). In this regard the present study has evaluated the hypertensive status of elderlies and observed their contextual variables.

Materials and Methods

With a cross sectional study design this study has been carried out among elderlies aged 60 years or older living in a selected area of Mohammadpur Thana of Dhaka district from January to December 2019. Following availing ethical approval from the concerning authority, study respondents were selected through cluster sampling technique.

Assessment of hypertension: In this study, the blood pressure was defined as high, following the JNV VI classification¹¹ on evaluation of their medical records.

Data collection and analysis: Each participant was approached after taking their informed written consent. Face to face interview was conducted to collect data in a structured questionnaire. Data regarding the sociodemographic background, modifiable risk factors and hypertensive profile, have been assessed and recorded. Statistical analysis has been carried out with the use of IBM Software- Statistical package for Social Science (SPSS) version 25.

Results

As observed from this study, hypertension was prevalent among 51 respondents (48.57%) and 54 (51.53%) respondents were normotensive. Among the sociodemographic attributes, the age group of 70 years and above found to have 56.4% of the hypertensive respondents compared to 43.6% normotensive respondents and the age group of below 70 years had 43.9% of hypertensive respondents compared

to 56.1% of normotensive respondents ($p>0.05$). Male respondents found to be more affected by hypertension (52.3%) than female respondents (45.9%) compared to their normotensive counterparts ($p>0.05$). With the increase of educational level, the prevalence of hypertension found to be significantly increased among the respondents ($p<0.05$). Respondents not being occupied with a job (home-maker or retired) also tend to have hypertension significantly higher than the respondents who were occupied with jobs ($p<0.05$). With the increase of monthly family income, the prevalence of hypertension found to have raised though this association was not significant ($p>0.05$). Respondents from joint family and who had higher number of family members showed to have higher prevalence of hypertension ($p>0.05$). Elderlies living in concrete-built houses showed to have higher prevalence of hypertension than them who were living in semi-concrete houses ($p>0.05$) (Table I).

Respondents who were overweight tend to have higher prevalence of hypertension (42.4%) than the respondents who were with normal weight (32.3%) ($p<0.05$). Respondents who have the record of doing regular exercise showed to have lower prevalence of hypertension (20.0%) than the respondents who didn't used to do exercise on regular basis (57.5%) ($p<0.05$). In this study, among the smokers and nonsmokers the prevalence of hypertension was nearly similar though slightly less among smokers ($p>0.05$). (Table II).

Discussion

Maintaining a healthy lifestyle is a pre-requisite to prevent and control hypertension (12). Routine evaluation for high blood pressure can be proven as a mainstream method to prevent the cardiovascular consequences among elderlies (13). In this study, the prevalence of hypertension among the study participants

was 48.57% which corresponds with another study in our country where they found the prevalence of hypertension among the 60 years and above age group at 53% (14). According to the observation from this study, among the sociodemographic background, hypertension was associated with the educational status and occupational status of the respondents, where with the increase in the educational level and not being occupied with a job found to have higher prevalence of hypertension ($p<0.05$).

Among the modifiable risk factors, respondents who were overweight and obese and not exercising regularly found to have significantly higher proportion of hypertension ($p<0.05$). Shukuri et al. in their study also found that being overweight and obese is a risk factor of hypertension among elderlies (4). Additionally, research studies have repeatedly observed the beneficial impact of doing regular exercise to have control over the blood pressure (15,16). Physical activity has been known to reduce cardiovascular complications and mortality among elderlies (17).

Regular intake of anti-hypertensive medications is also of prior concern to manage hypertension among elderlies and also to reduce cardiovascular consequences among them (18). This study has observed that, all of the hypertensive respondents were taking anti-hypertensive medication among whom 13.7% gave history of irregular intake and they mainly faced financial issue to maintain the regularity of drug intake. Angiotensin receptor blocker/inhibitor were the most commonly taken drug (49.3%) for the management of hypertension according to this study. In the study of Kontsevaya et al. high cost was the reason for non-adherence to the prescribed anti-hypertensive medication for 21.7% of the respondents whereas, majority of the respondents in their study claimed of feeling well as the reason to not take the medicines regularly (19).

Table I: Sociodemographic Attributes of Hypertension Among Elderlies

		Hypertensive (n ₁ =51)	Normotensive (n ₂ = 54)	p value
Age (years)	60-69	29 (43.9%)	37 (56.1%)	0.217
	70 and above	22 (56.4%)	17 (43.6%)	
Gender	Male	23 (52.3%)	21 (47.7%)	0.519
	Female	28 (45.9%)	33 (54.1%)	
Educational status	Illiterate	13 (30.2%)	30 (69.8%)	0.004
	Primary	8 (57.1%)	6 (42.9%)	
	Secondary	8 (42.1%)	11 (57.9%)	
	Higher secondary Graduation and above	4 (80.0%) 18 (75.0%)	1 (20.0%) 6 (25.0%)	
Occupational status	Service holder	6 (75.0%)	2 (25.0%)	0.019
	Businessman	6 (54.5%)	5 (45.5%)	
	Day laborer	1 (8.3%)	11 (91.7%)	
	Home maker Retired	17 (44.7%) 21 (58.3%)	21 (55.3%) 15 (41.7%)	
Marital status	Have spouse	27 (43.5%)	35 (56.5%)	0.216
	Do not have spouse	24 (55.8%)	19 (44.2%)	
Monthly family income (taka)	8000-20000	10 (35.7%)	18 (64.3%)	0.241
	21000-50000	19 (48.7%)	20 (51.3%)	
	51000-80000	13 (52.0%)	12 (48.0%)	
	81000-100000	9 (69.2%)	4 (30.8%)	
Type of family	Joint	27 (50.0%)	27 (50.0%)	0.763
	Nuclear	24 (47.1%)	27 (52.9%)	
Number of family members	1-4	25 (45.5)	30 (54.5%)	0.545
	5-7	19 (48.7%)	20 (51.3%)	
	8-11	7 (63.6%)	4 (36.4%)	
Housing status	Concrete house	44 (52.4%)	40 (47.6%)	0.118
	Semi concrete house	7 (33.3%)	14 (66.7%)	

p value reached from Chi-square analysis (adjusted with Fisher's exact)

Table II: Modifiable risk factors and hypertension

		Hypertensive (n ₁ =51)	Non- hypertensive (n ₂ = 54)	p value
BMI	Underweight	0 (0.0%)	5 (100.0%)	0.000
	Normal	10 (32.3%)	21 (67.7%)	
	Overweight	14 (42.4%)	19 (57.6%)	
	Obese	27 (75.0%)	9 (25.0%)	
Regular exercise	Yes	5 (20.0%)	20 (80.0%)	0.001
	No	46 (57.5%)	34 (42.5%)	
History of smoking	Yes	27 (47.4%)	30 (52.6%)	0.788
	No	24 (50.0%)	24 (50.0%)	

p value reached from Chi-square analysis (adjusted with Fisher's exact)

Among the hypertensive group, duration of hypertension was between 1 to 10 years for 54.9% of the respondents and more than 10 years for 45.1% of the respondents. All of the hypertensive respondents gave history of taking anti-hypertensive medication. Among them, angiotensin receptor blocker/inhibitor were taken by 49.3%, beta blockers were taken by 29.9%, calcium channel blocker was taken by 14.9%, diuretics was taken by 3.0% and alpha blockers was taken by 3.05%. Regular drug intake was claimed by 86.3% of the respondents. Among the respondents who didn't used to intake medicines regularly, financial issue was the main issue among them (57.1%) (Table III).

care cost and challenges in personal, familial and national level. This study found educational status, occupational status, BMI and exercising to be significantly associated with hypertensive status of the respondents. With the increase of the educational attainment, not being occupied, being obese and overweight and not doing exercise regularly found to be related with higher prevalence of hypertension among the elderlies. Further in depth studies are suggested to understand the mechanism that, how these factors increase the hypertension among the old age population, thus health awareness and action planning can be incorporated from younger age to prevent the incidence of hypertension and its associated co-morbidities among the aging population.

Table III: Hypertensive history of the patient (n =51)

		Frequency	Percentage
Duration (years)	1-10	28	54.9%
	>10	23	45.1%
Type of drug	Angiotensin receptor blocker/inhibitor	33	49.3%
	Beta-blocker	20	29.9%
	Calcium-channel blocker	10	14.9%
	Diuretics	2	3.0%
	Alpha-blocker	2	3.05%
Regular intake of drug	Yes	44	86.3%
	No	7	13.7%
Cause of irregularity in drug intake	Don't think drug is necessary	1	14.3%
	Too expensive	1	14.3%
	Blood pressure is now normal	1	14.3%
	Lack of money	4	57.1%

Conclusion

Hypertension is an established risk factor for many health issues, prevention and control of which can reduce the associated disability adjusted life years. Ensuring a sound and healthy old age through proper management of high blood pressure can moderate the health

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A Case Report on rtQ215H Mutation in association with hepatocellular carcinoma among A Bangladeshi Hepatitis-B Chronic Carrier.

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Abstract

Background: Hepatitis B virus (HBV) continues to pose a heavy burden in Bangladesh. Its high rate of natural mutations, such as rtQ215H, may influence not only drug resistance but also long-term health outcomes. **Aim:** To present a case highlighting the clinical impact of the rtQ215H mutation in an untreated chronic hepatitis B (CHB) patient. **Methods:** A 58-year-old Bangladeshi man with untreated CHB underwent HBV DNA quantification, serology, and sequencing of the polymerase gene. His clinical course was followed. **Results:** The rtQ215H mutation was found in the reverse transcriptase region. Though initially stable and with improved liver enzymes on lamivudine, the patient tragically developed hepatocellular carcinoma (HCC) within three years and died soon after. **Conclusion:** This case humanizes the risk behind HBV mutations. Even without prior therapy, rtQ215H may contribute to HCC development. Careful genetic monitoring of CHB patients is essential for early guidance and better outcomes.

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Keywords: HBV, rtQ215H, polymerase mutation, untreated CHB, hepatocellular carcinoma.

Introduction

Hepatitis B virus (HBV) is a DNA virus from the Hepadnaviridae family. It is a major etiological agent of infectious hepatitis. Clinical pictures of this virus infection ranging from asymptomatic infection to complete resolution or acute fulminant to chronic hepatitis that may lead to life threatening condition, such as, liver cirrhosis (LC) and hepatocellular carcinoma (HCC) (1). Despite the availability of a safe, effective vaccine against HBV since 1982, infection still remains a major health problem. Globally, about 240 million people are chronic HBV (CHB) carrier and more than 780,000 people die due to acute and chronic consequences of infection in each year (2). Bangladesh belongs to the intermediate prevalence country of HBV infection.³ In this region, about 5%-6% of apparently healthy individuals are chronic carrier and most of them are unaware of their presence of infection (4,6). The lifetime risk of acquiring HBV infection is about 20% to 60% (7). Previous studies showed that HBV is responsible for 31.25% cases of acute hepatitis and 76.3% cases of chronic hepatitis, 61.15% cases of cirrhosis of liver and 33.3% cases of HCC in Bangladesh (8,10).

The rate of HBV replication among these chronic patients is considerable, about more than 10⁸-10¹¹ viral particles per day (11). As reverse transcriptase (RT) enzyme of HBV Pol gene lacks proof reading capacity, HBV replication is also associated with a high mutational rate of 10⁵ substitutions /base /cycle (12). Thus, all possible single base changes in the HBV genome are generated daily and chance of antiviral resistant HBV mutant development in untreated CHB patients (8). There is a concern that antiviral resistant HBV found up to 10% to 15% of untreated CHB patients (8,13). Besides that, different controlling approaches like vaccination and antiviral therapies create selective pressure on HBV

genome result in antiviral resistant strains. The genomic changes are stable and these resistant viruses are transmitted to another individual (14).

Case Report

On 2014, we found a 58 years male untreated CHB patient at the department of Virology, BSMMU, when he came for his HBV DNA routine laboratory test. The patient was HBeAg negative and serum SGPT was 42 U/L. The viral load of this patient was 2.85×10⁵ IU/ml. We did molecular study of this HBV DNA which showed rtQ215H mutation in the reverse transcriptase domain of the HBV Pol gene. This region is critical for antiviral action. After that, the patient was treated by lamivudine (Hepavir 100 mg/day, Square Pharmaceuticals Ltd., Bangladesh) from March 2014 to April 2017 and his SGPT became normal. In 2017, we again interviewed this patient and we found he diagnosed a case of HCC. After that, patient had expired within a month.



Figure 1: Mutation prediction of antiviral resistance mutation in HBV genotype C*.

Note: Circle in figure indicates mutation. Mutations were identified by the alignment of all obtained HBV Pol protein with respective genotype positive reference sequences from NCBI gene bank through BioEdit software. Figure 1 shows mutation as rtQ215H in the reverse transcriptase domain of HBV the Pol gene.

Discussion

The emergence of natural mutations in the HBV genome should be expected due to characteristics of its genome. The major causes of mutations in association with antiviral resistance include some viral factors, such as, high kinetics of viral replication and clearance, and the lack of a proofreading mechanism during reverse transcription by RT enzyme, which creates many mutants of HBV (15). Antiviral resistance designates the presence of a unique nucleotide and the corresponding amino acid mutations in the antiviral target gene that have been previously reported as associated with antiviral resistance (16). These genomic mutations are stable and resistant viruses can be transmitted to another individual which is a significant public health risk (7). Thus, our study strongly demands to document the antiviral resistance mutations of HBV among untreated Bangladeshi CHB patients. Antiviral resistance mutations present as primary and compensatory or secondary type of mutations.

Primary resistance mutations decrease sensitivity to antiviral agents (17). While, the compensatory mutations restores the functional defects in viral polymerase activity that gains replication capacity of that resistant virus and increases resistance to antiviral agents (16,17). Commonly reported primary resistance mutations are A181V, A181T, T184G, A194T, S202I, N236T, M204V, M204I and M250V. The major secondary/compensatory mutations are L80V, L80I, L180M, rtI169T, V173L, rtQ215H/S (18,19, 20). Other proposed compensatory mutations are rtV84M, rt214, rtL217P, rtL229M, rtI233V, rtN238H (21).

We found that HBV showed single antiviral resistance mutation as rtQ215H in an untreated patient. Sayan et al showed that compensatory mutations at rtQ215A/H/P/S found as naturally developing mutations in untreated CHB patients (22). Further researches reported that frequent mutations had found at rtQ215 in both untreated and lamivudine/adefovir treated patients.23, 24 Earlier published data also suggested that these amino acid changes at codons: rt214, rt215, rt221 and rt238 reduce efficacy to adefovir and lamivudine, and these mutation are marked as adefovir secondary/compensatory resistance mutations (25,26,27). A case report by Micco et al. also reported that polymorphism in rtQ215H causes primary resistance to adefovir found in a lamivudine resistant and adefovir non-re-

sponsive CHB patient (28). This finding suggests that mutation at rtQ215H could be responsible for primary resistance to adefovir, or reduced sensitivity to adefovir. On the contrary, Olyaei et al. reported that HBV Pol gene mutations in the rtQ215 locus are frequently found in the untreated CHB patients (24). This author suggested that the rtQ215 changes do not affect HBV replication and do not cause antiviral resistance to adefovir or lamivudine but poses higher risk liver disease progression and it may be represented as the polymorphisms rather than resistance mutations (24). When we interviewed this rtQ215H mutation positive patient, we found the patient was further treated by lamivudine and his SGPT became normal. However, we do not know if this mutation is responsible for adefovir resistance or not. Interestingly, this patient developed HCC in the year of 2017 and died soon after. Therefore, it is suggested that polymorphisms and mutations of codon 215 should be carefully monitored by physicians for their relevance to therapy failure and disease progression.

Limitations Of Study

We observed this patient by interviewed over phone call and not take opportunity for direct supervision.

Conclusion

In conclusion, HBV could be shown rtQ215H mutation among the untreated patients. This mutation may not be responsible for antiviral resistance rather it could be complicated with HCC. Therefore, mutations in the 215 region of the RT domain HBV Pol gene among the CHB patients should be carefully monitored by physicians for their relevance to therapy failure and disease progression.

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