

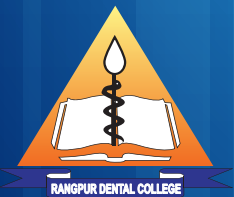
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Vitamin D on diseases and immunity

Begum S¹

Vitamin D is a vital nutrient, helping the gut to absorb calcium while keeping calcium and phosphate at the right concentrations by depositing calcium into the collagen matrix to support healthy bone and teeth. There are two types of vitamin D, which are known as D-2 and D-3. D-3 (25-hydroxy vitamin D) is real vitamin D-produced naturally through our skin. One study found that D3 is 87 percent more effective than D2, and is the preferred form for treating vitamin D deficiency. Vitamin D is not naturally present in many foods. Instead, the bulk of our requirement is synthesized in the skin after exposure to ultraviolet light from the sun. Recommended dose vary from 400 IU to 800 IU daily. All guidelines unanimously agree that serum levels of 25-hydroxyvitamin D (25OHD) <25 nmol/l (10 ng/ml) should be avoided at all ages.

Severe deficiency causes bone pain, muscle pain, abnormality in tooth development causing brittleness of tooth and more prone to caries. Vitamin D isn't actually a vitamin, although scientists refer to it as such. It's actually a steroid hormone and is also related to serotonin and melatonin for that reason deficiency of this causes depression and sleep disturbance. There are only about 30,000 genes in our body and vitamin D has been shown to influence about 3,000 of them. That is one of the primary reason it influences so many diseases, from cancer and autism to heart disease and rheumatoid arthritis, just to name a few.

It has been found that around 1 billion of the total world population is suffering from vitamin D deficiency which is more in south Asian about 80%. One study found that more than 40 percent of the U.S. populations were vitamin D deficient. In Bangladesh the women and the urban peoples are more suffering from vitamin D deficiency due to lack of

sun exposure. That's why some authors have referred to vitamin D deficiency as a pandemic. 60 percent of people with type 2 diabetes have vitamin D deficiency. Studies showed very low levels of vitamin D among children, the elderly and women. Now Vitamin-D deficiency is the Global Health Issue.

The level of Vitamin D in blood matters but not the dosages. So it is more important to monitor vitamin D level on regular basis. Vitamin D has a protective effect against cancer in several ways, including: Increasing the self-destruction of mutated cells, reducing the spread and reproduction of cancer cells, causing cells to become differentiated and reducing the growth of new blood vessels from pre-existing ones, which is a step in the transition of dormant tumors turning cancerous.

Vitamin D regulates the expression of genes that influence immune system to attack and destroy bacteria and viruses. A new global collaborative study has confirmed that vitamin D supplementation can help to protect against acute respiratory infections and flu.

In Bangladesh even educated persons are suffering from deficiency of vitamin D due to lack of awareness and neglecting this important health issue. Health related personnel's should be more concerned about this global issue and public awareness program will play an important role in communicating mass people.

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Socio-Demographic and Clinical Characteristics of Type 2 Diabetes Mellitus Patients at Two Tertiary Level Hospitals in Mymensingh

Shaha KC¹, Rahman AKMS², Parvin N³, Sifat E⁴, Khan MM⁵

Abstract:

Background: Diabetes mellitus is one of the oldest diseases known to man, which was the first reported in Egyptian literature about 3000 years ago. The higher prevalence was found in urban areas predominantly among women. Urbanization and urban migration have been established as a risk factor for an increased occurrence of diabetes. **Objective:** The aim of the present study was to evaluate the socio-demographic and clinical characteristics of type 2 diabetic patients at two tertiary level hospitals in Mymensingh. **Methods:** A descriptive, cross sectional study was conducted from July 2015 to December 2015 among patients attending at Medicine Outpatient Department of the Community Based Medical College Hospital, and Endocrine Outpatient Department of the Mymensingh Medical College Hospital. Data were collected through the interviewing of the patients. The collected data were entered into the computer and analyzed by using SPSS (version 20.1). The study was approved by the institutional ethical committee. **Results:** In a pool of 300 type 2 diabetics, more than half were female (n=223, 74.3%). More than half (57.3%) of the respondents were in the middle age group (41-60 years). Less than half (35.7%) of the patients were overweight. Out of 300 patients, 197 patients came from urban area and 103 patients from rural area. More than half (50.7%) of the patients were illiterate. The highest numbers (214, 71.3%) of patients were housewives. 56% patients had the family history of diabetes mellitus. Most of the patients (48.3%) had a history of diabetes mellitus for less than 5 years. About 79 (26.3%) patients on anti-diabetic drugs had controlled optimal glycemic levels. The Benedict test result was positive for 203 patients. **Conclusion:** Females are more prone to develop type 2 diabetes mellitus compared to males. The present study revealed that obesity, family history of diabetes mellitus and uncontrolled glycemic status were highly prevalent in type 2 diabetes mellitus subjects.

Key words: Diabetes mellitus, Co-morbid condition.

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Introduction:

Human health and disease are unequally distributed through-out populations. When specific diseases, adverse health outcomes, or other health characteristics are more prevalent among one group than another group, or more prevalent in one country than in another, the logical question that follows is "Why?" To answer the question "Why," one must consider "three Ws"-who was affected?

Where did the event occur? When did the event occur¹? Diabetes mellitus is one of the oldest diseases known to man, which was the first reported in Egyptian literature about 3000 years ago. The higher prevalence was found in urban areas predominantly among women. Urbanization and urban migration have been established as a risk factor for an increased occurrence of diabetes. The trend has been authenticated by the World Health Organization (WHO)².

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There is strong evidence that modifiable risk factors such as obesity and physical inactivity are the main non genetic determinates of the disease. Obesity plays an important role for the increasing burden of diabetes in the developed world. Type 2 diabetes is much more common and accounts for around 90% of all diabetes cases worldwide. It is most frequently in adults but is being observed increasingly in adolescents as well³. This study undoubtedly benefits the physicians for prevention of diabetes mellitus in the future.

Materials & method:

A descriptive, cross sectional study was conducted from July 2015 to December 2015 among patients attending at Endocrine Outpatient Department of the Mymensingh Medical College Hospital and Medicine Outpatient Department of the Community Based Medical College Hospital after obtaining requisite consent from the patients. The interviews were held directly in the corridor just outside the medical Outpatient Department. Height and weight of the patients were measured to calculate BMI. After taking informed consent and informing details about the procedure, 2 hours after breakfast blood glucose level of patients was assessed by glucometer.

Then mid stream urine sample from the patients was collected and Benedict test was performed in experimental pharmacology room of Mymensingh medical college. The collected data were entered into the computer and analyzed by using SPSS (version 20.1).

Results:

According to table I, Most of the patients (57.3%) belonged to the middle age group 41-60 years. More than half of the respondents were female (n=223, 74.3%). Out of 300 patients, 197 patients came from urban area and 103 patients from rural area. Most of the patients (50.7%) were illiterate. Among 300 patients, 145 (48.3%) patients had a history of diabetes mellitus less than 5 years, According to table II, Most of the patients (71.3%) were housewives. According to figure 1: 168 patients (56%) had the family history of diabetes mellitus. According to table III, More than half (50.3%) of the patients had normal BMI level and 35.7% patients were overweight. According to table IV, about 79 (26.3%) patients on anti-diabetic drugs had controlled optimal glycemic levels while 221 (73.7%) patients had uncontrolled glycemic level. According to table 5, among 300 cases, the color of Benedict's reagent remained blue for 97 (32.3%) patients which indicate

negative result, and the color turned to green for 56 (18.7%) patients, yellow for 43 (14.3%) patients, orange for 57 (19.0%) patients, and brick red for 47(15.7%) patients, all of which indicate positive result.

Table I: Demographic characteristics of the study population (n=300)

Parameters	Frequency (%)
Age	
40 years	77 (25.7)
41-60 years	172 (57.3)
> 60 years	51 (17.0)
Total	300 (100)
Sex	
Male	77 (25.7)
Female	223 (74.3)
Total	300 (100)
Residence	
Urban	197 (65.7)
Rural	103 (34.3)
Total	300 (100)
Educational status	
Primary	72 (24.0)
Junior	25 (8.3)
Secondary	21 (7.0)
Higher secondary	15 (5.0)
Graduated	15 (5.0)
Illiterate	152 (50.7)
Total	300 (100)
Duration of diabetes	
< 5 years	145 (48.3)
5-10 years	102 (34.0)
>10 years	53 (17.7)
Total	300 (100)

Table II: Occupational status of the study population (n=300)

Occupation	Frequency (%)
Service Holder	27 (9.0)
Businessman	17 (5.7)
Retired	21 (7.0)
Farmer	11 (3.7)
Unemployed	10 (3.3)
Housewife	214 (71.3)
Total	300 (100)

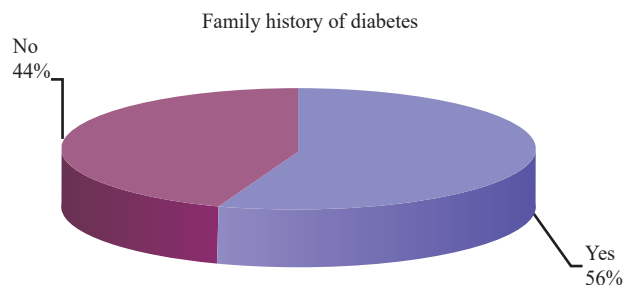


Figure 1: Pie chart showing family history of diabetes mellitus of the patients.

Table III: Body mass index of the study population (n=300)

Body mass index	Frequency (%)
Under weight	20 (6.7)
Normal	151 (50.3)
Over weight	107 (35.7)
Obese	21 (7.0)
Morbidly obese	01 (0.3)
Total	300 (100)

Table IV: Assessment of 2 hours after breakfast blood glucose level (n=300)

2 hours after breakfast	Frequency (%)
<10 mmol/L (controlled)	79(26.3)
10-15 mmol /l (Uncontrolled)	115(38.3)
15.1-20 mmol/l (Uncontrolled)	73(24.3)
>20 mmol/l (Uncontrolled)	33(11.0)
Total	300(100)

Table V: Distribution of type 2 DM patients according to Benedict's test (n=300)

Benedict test	Frequency (%)
Blue (Negative)	97(32.3)
Green (+)	56(18.7)
Yellow (++)	43(14.3)
Orange (+++)	57(19.0)
Brick red (++++)	47(15.7)
Total	300(100)

Discussion:

This study showed that diabetes mellitus is more prevalent in female patients than in male patients. This may be assigned to the fact that women are more obese than men. Similar results were found in the study of Alam et al. (2014), Mann et al. (2009) and Abebaw et al. (2016)³⁻⁵. This study also found a higher prevalence of diabetes was among middle aged patients, with a high percentage (57.37%) in the age group of 41-60 years. This result correlates with the study of Sajith et al. (2014)⁶. This study showed that 56% patients suffered from type 2 diabetes mellitus due to genetical reasons and the remaining due to unknown cause. Near to similar results were obtained in the study conducted by Valdez et al., where 51% patients had a positive family history suggesting the role of co-existing factors⁷. In the present study, type 2 DM is more common in urban people (34.3%). Our study findings are also similar to the study conducted in Bangladesh by Akter et al. (2014)⁸. Diabetes may be more common among urban residents due to sedentary life style or different dietary habits. In our study, majority, 214 (71.3%), of the participants were housewives and service holder, 27 (9.0%). This present study correlates with the study of Abebaw et al. (2015) but the percentage is not same⁵. In their study they observed that majority, 98 (34%), of the participants were housewives and government employee, 50 (17.4%). Obesity is the important risk factor for type 2 DM. In the present study 35.7% patients were overweight. Dissimilar results were obtained in the study conducted by Daousi et al. (2005)⁹. They reported that 86% patients with type 2 diabetes were overweight. This variation occurs due to differences in dietary habits. Low education is another risk factor for developing diabetes mellitus. A study conducted by Shrestha et al. (2013) reported 44% patients were illiterate, which is slightly lower compared to this study (50.7%)¹⁰. The duration of diabetes plays an important role in management of diabetes. This study showed that most of the patients (48.3%) had a diabetic history of less than 5 years. Near to similar results were obtained in the study conducted by Sajith et al., where 43.81% patients had a diabetic history of less than 5 years⁶. In this study about 26.3% patients on anti-diabetic drugs had controlled optimal glycemic levels while 73.7% had uncontrolled glycemic levels. Our present study does not correlate with the study of Agarwal, Jadhav and Deshmukh¹¹. In their study they reported that 41% patients on anti-diabetic drugs had controlled optical glycemic levels, while 59% had uncontrolled glycemic level.

Conclusion:

Females are more prone to develop type 2 diabetes mellitus compared to males. The present study revealed that obesity, family history of diabetes mellitus, uncontrolled glycemic status and co-morbidity were highly prevalent in type 2 diabetes mellitus subjects. So continuous patient education and awareness program are required.

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Age related changes in oxidative stress status

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Abstract:

Background: Ageing is one of the nature's most complex biological phenomena. Accumulation of oxidative damage might be responsible for the ageing process. **Objective:** The present study was to find out the relationship between oxidative stress status and ageing. **Methodology:** The study was performed at the department of Physiology, Rajshahi Medical College during the period of July 2013 to June 2014. A cross-sectional and comparative study was carried out in a sample of 45 healthy adult subjects of both gender; 18-21 years (n=23) and 41-68 years (n=22). Malondialdehyde (MDA), a lipid peroxide and alpha-tocopherol, an anti-oxidant in plasma was measured. It was used MDA: alpha-tocopherol ratio as reliable marker of oxidative stress status due to higher correlation coefficient than MDA and alpha-tocopherol concentration alone. **Results:** There was a significant age related increase in oxidative stress status ($p < 0.05$). In addition, there was no significant difference of anti-oxidant status between below and above forty years male group but anti-oxidant status was significantly higher in below forty years female group than above forty years female group. **Conclusion:** Below forty years female group had the lowest oxidative stress and the highest anti-oxidant defense. However it is necessary to carry out cross-longitudinal studies in cohort to confirm our findings.

Key words: Age related changes, Oxidative stress status, Malondialdehyde.

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Introduction:

Oxidative stress results from the imbalance between oxidative and anti-oxidative mechanisms with increased levels pro-oxidants and depletion of anti-oxidants leading to tissue damage¹. With age and increasing oxidative stress, endogenous antioxidant systems may be challenged beyond their ability to maintain the pro-oxidant to anti-oxidant equilibrium².

Oxidative damage to DNA, proteins and lipids induced by the overproduction of reactive oxygen species (ROS) accumulate with age and contributes to degenerative diseases and the aging phenomenon by disrupting cellular homeostasis. On the other hand, the human body generally has anti-oxidant system which plays an important role in the suppression of ROS over production and protects cells from

oxidative stress. Anti-oxidant system is comprised of endogenous compounds (billirubin, uric acid, super oxide dismutases, catalase, glutathione peroxidase etc.) and exogenous compounds (carotenoids, tocopherols, ascorbate, bioflavonoids etc.) Suresh et al. (2010) state that lipid peroxidation increases in elderly people when compared to normal young subjects¹. But Andriollo-Sanchez et al. (2005) state that lipid peroxidation is significantly higher in middle aged group than in the older group³. In contrast, Suzuki et al. (2010) state that both lipid peroxide and vitamin E tocopherols are lower in centenarians⁴. In addition, Kasapoglu and Ozben (2001) found no age and gender differences of vitamin E levels⁵. On contrary, Mendoza-Nunez et al. (2007) found age related decrease of total antioxidant status⁶.

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So the results of the studies are conflicting and are not conclusive. So we aimed to verify the hypothesis that a direct relationship exists between oxidative stress and aging, to establish the possible age related differences in oxidative stress status and to correlate between anti-oxidant status (vitamin E) with pro-oxidant status (MDA).

Methods:

This cross-sectional comparative study was carried out in the department of Physiology, Rajshahi Medical College between the periods of January 2013 to June 2014. Forty five healthy adult subjects of both gender: 18-21 years (n=23) and 41-68 years (n=22) were enrolled in the study. Study subjects were selected by systematic sampling technique from medical students, doctors and staffs of Rajshahi Medical College. The protocol of the study was approved by the Ethical Review Committee (ERC) of Rajshahi Medical College. All the subjects were free from Diabetes, Hypertension, Chronic liver and renal disease, Alcoholism and Smoking. Persons taking antioxidant therapy or other drugs, pregnant and lactating women were excluded from the study. Before recruitment, aim, benefit and procedure of the study was explained and informed written consent was taken from each study subject. Thorough physical examinations of all subjects were done. Then under aseptic precaution, 4 ml blood was taken from each subject in a test tube containing anti-coagulant di-potassium EDTA. Plasma was separated after centrifuging for 15 minutes at 3000 rpm. Then plasma Malondiladehyde (MDA) and plasma alpha-tocopherol levels were estimated.

Measurement of MDA:

Half ml plasma was mixed with 2.5ml of 20% trichloroacetic acid and after 10 min; the sample was centrifuged (3500×g for 10 min). The precipitate was washed with sulfuric acid (0.05mol/liter) and treated in a test tube with 2.5ml of sulfuric acid and 3ml of thiobarbituric acid (TBA) reagent (2.0gm TBA/l in 2mol sodium sulfate/liter). The test tube was placed in boiling water bath for 30 min and cooled in running tap water. The TBA reactive material was mixed with 4ml n-butanol and centrifuged (3500×g for 10 min). A standard of MDA was treated similarly. The optical density (O.D) of n-butanol extract of plasma and MDA standard was measured at 532 nm against a butanol blank by spectrophotometer. The result was expressed as μmol MDA/liter of plasma. (Das et al., 1990)⁷.

Measurement of alpha-tocopherol:

Three stoppered centrifuge tubes were taken. One and half ml plasma, standard and water (blank) were measured and were taken in each tube respectively. To the test and blank, 1.5 ml ethanol was added and to the standard, 1.5 ml water was added. 1.5 ml xylene was added to each tube, stoppered, mixed well and centrifuged. 1.0 ml of each xylene layer was transferred into a clean stoppered tube, carefully excluded any protein or ethanol. 1.0 ml dipyrindyl reagent was added to each tube, stoppered and mixed. 1.5 ml of the mixture was taken into colorimeter cuvettes and the absorbance (A460) of the test and standard was read against the blank at 460 nm. Then in turn, beginning with blank, 0.33 ml ferric chloride solution was added, mixed, the wave length was set to 520 nm and 1.5 min after mixing, the absorbance (A520) of the test and standard was read against the blank at 520 nm. The result was expressed as mg of alpha-tocopherol/deciliter of plasma (Baker and Frank,1968)⁸. Data was analyzed by computer using SPSS software program. Statistical analysis was done by paired t-test. P value less than 0.05 was taken as significant. Pearson's correlation coefficient was determined between the measured parameters at 5% level of significance.

Results:

Mean plasma MDA level was significantly higher, mean plasma Alpha-tocopherol level was significantly lower and mean MDA: Alpha-tocopherol ratio was significantly higher in above forty years age group than below forty years age group (Table I).

Table I: Plasma Malondiladehyde and Alpha-tocopherol concentration in different age groups (n=45)

Parameters	Below 40 years group (n =23)	Above 40 years group (n =22)	P value
Malondialdehyde (micro-mol/liter)	2.80±0.71	3.42±0.46	< 0.05
Alpha-tocopherol (mg/dl)	2.51±0.84	1.68±0.79	< 0.05
Malondialdehyde: Vitamin E ratio	1.28±0.74	2.45±1.57	< 0.05

Data expressed as Mean±SD. Statistical analysis were done by student's unpaired t-test.

Mean plasma MDA level was significantly higher, mean plasma Alpha-tocopherol level was not significantly

different and mean MDA: Alpha-tocopherol ratio was significantly higher in above forty years male group than below forty years male group (Table II).

Table II: Plasma Malondialdehyde and Alpha-tocopherol concentration in different male age groups (n=25)

Parameters	Below forty years male (18-21 years) (n=10)	Above forty years male (41-68 years) (n=15)	P value
Malondialdehyde (micro -mol/liter)	2.49±0.91	3.36±0.46	< 0.05
Alpha -tocopherol (mg/dl)	2.12±1.04	1.48±0.62	> 0.05
Malondialdehyde: Vitamin E ratio	1.52±1.07	2.82±1.74	< 0.05

Data expressed as Mean±SD. Statistical analysis were done by student's unpaired t-test.

Mean plasma MDA level was significantly higher, mean plasma Alpha-tocopherol level was significantly lower and mean MDA: Alpha-tocopherol ratio was significantly higher in above forty years female group than below forty years female group (Table III).

Table III: Plasma Malondialdehyde and Alpha-tocopherol concentration in different female age groups (n=20)

Parameters	Below forty years female (18-21 years) (n=13)	Above forty years female (41-68 years) (n=07)	P value
Malondialdehyde (micro -mol/liter)	3.03±0.42	3.54±0.48	< 0.05
Alpha-tocopherol (mg/dl)	2.82±0.50	2.11±0.98	< 0.05
Malondialdehyde: Vitamin E ratio	1.09±0.25	2.07±1.07	< 0.05

Data expressed as Mean±SD. Statistical analysis were done by student's unpaired t-test.

Age was positively correlated with plasma MDA level and plasma MDA: Alpha-tocopherol ratio and negatively correlated with plasma Alpha-tocopherol level (Table IV).

Table IV: Correlation between the Age and oxidative stress markers (n=45)

Parameters	r value	Strength of association
AGE and MDA	+0.43	Weak positive
AGE and VITAMIN E	-0.48	Weak negative
AGE and MDA: VITAMIN E ratio	+0.57	Moderate positive

Correlation between age and oxidative stress markers was calculated using pearson's correlation test.

Discussion:

An imbalance in redox state where pro-oxidants overwhelm antioxidant capacity results in oxidative stress. Human studies have suggested that oxidative stress status alters according to age¹, sex⁹, life style¹⁰, habit¹¹, BMI¹ and calorie intake¹². The role of free radical and oxidant injury has been repeatedly described in various diseases but rarely healthy people. So this study first examines biochemical parameters of ageing on healthy human subjects and shows significance in alteration. We have measured markers of oxidative stress status in healthy adults below and above forty years age group. We have accepted forty years age as demarcation point because consequences of ageing like weight gain, presbyopia and appearance of wrinkles etc. commences after forty years.

Direct measurement of free radicals is difficult due to their unstable and transient nature; therefore the tendency of free radicals to cause lipid peroxidation has been used as an indirect measure. Malondialdehyde (MDA) is a three carbon, low molecular weight aldehyde that can be produced from free radical attack on polyunsaturated fatty acids of biological membranes¹. So the determination of MDA is used for monitoring lipid peroxidation in this study.

We have found plasma MDA levels were significantly higher in the group of persons above forty years as compared with the below forty age group. This finding is consistent with the studies of several researchers^{1,13-16}. Two possible factors may have contribution to the increased lipid per oxidation: the increasing production of free radicals and the declining activity of the antioxidant system. However Mendoza-nunez et al. (2005) reported that significant increase of lipid peroxide only in subjects more than sixty years of age in comparison with the younger age group⁶. This finding against our's may be related to different population.

We have measured vitamin E as anti-oxidant marker because it is major lipid soluble chain breaking antioxidant which prevents lipid peroxidation. Vatassery et al. (1983) state that Alpha and gama tocopherol accounted for nearly all of the vitamin E compounds in plasma and platelet samples. The mean gama tocopherol concentration was one-fourth of that of alpha in both plasma and platelets. Moreover gama tocopherol is only thirteen percent as active as alpha tocopherol¹⁷.

So the direct conclusion would be that the contribution of gamma tocopherol to the vitamin E nutritional status in human is relatively negligible compared with alpha tocopherol. So we have measured alpha tocopherol as active component of vitamin E.

We have found plasma alpha-tocopherol levels were significantly lower in the group above forty years as compared with the below forty years age group. It shows that anti-oxidant defense decreases with advancing age. This finding is in accordance with the studies of^{3,6}. However Mendoza-nunez et al. (2007) found no age related change in oxidative stress markers in subjects less than sixty years⁶. This variation may be due to different population and life style factors.

Suzuki et al. (2010) state that both lipid peroxide and vitamin E tocopherols were lower in centenarians⁴. Since tocopherols are lipid soluble, it is also possible that very old persons, who generally have low blood lipids, display artificially low blood tocopherol levels since it is mainly lipid bound.

Kasapoglu and Ozben (2001) state that vitamin E level does not change with age and there is also no gender difference⁵. Their data suggest that the level of oxidative stress increase can not entirely be attributed to a decrease in the activities of anti-oxidant defense system and probably various factors may contribute to this process.

We have used Malondialdehyde: alpha -tocopherol ratio as marker of oxidative stress status instead of Malondialdehyde or alpha-tocopherol concentrations alone because oxidative stress is the imbalance between the pro-oxidants and the anti-oxidants. In addition, we have found that the correlation coefficients were higher for MDA: alpha-tocopherol ratio than MDA or alpha-tocopherol concentrations alone.

We have found oxidative stress was more in above forty years group than below forty years group which supports the free radical theory of ageing. This finding is compatible with the findings of several researchers^{1,16,18}. However Andriollo-Sanchez et al. (2005) state that plasma MDA levels were significantly higher in middle age group than the older group. They opine that MDA production is dependent on polyunsaturated fatty acid intake, and it can not be ruled out that a possible lowered consumption of polyunsaturated fatty acids by older elderly which resulted in a lesser extent of lipid peroxidation³. However, it may be due to lack of physical activity in older elderly in comparison to middle age group.

We have found MDA levels were significantly higher in above forty years male group than below forty years male group but there was no significant difference of plasma alpha-tocopherol levels. As a result, oxidative stress was significantly higher in above forty years male group than below forty years male group. It points out that neither ageing process nor sex hormone affect anti-oxidant defense mechanism in male subjects. On the other hand, we have found MDA levels were significantly higher and plasma alpha-tocopherol levels were significantly lower in above forty years female group than below forty years female group. As a consequence, oxidative stress was significantly higher in above forty years female group than below forty years female group. It indicates that female sex hormones are protective against oxidative stress which are higher in young women.

One of the strength of our study is we have measured two closely inter-related biomarkers of oxidative stress status. However it was a cross-sectional study. Therefore it is necessary to carry out cross-longitudinal studies in cohort to confirm our findings.

Conclusions:

This study confirms the intensification of oxidative stress during ageing. So dietary intake of a variety of antioxidants might be beneficial for preserving the normal function in elderly people.

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Management of Medical Record Keeping in a Tertiary Level Government Hospital - A Cross Sectional Study

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Abstract:

Background: Medical record management has become an integral activity of the hospital management. The department provides multiple benefits not only to the patients but also to running a hospital efficiently.

Objectives: To assess the different management aspect of medical record keeping such as the completeness of medical record with its important contents, medical record management status according to the statement of the respondents related to medical record management, the problems faced by the respondents during duty associated with the medical record management and the suggestions for necessary improvement of medical record keeping practice. **Methodology:** A descriptive type of cross sectional study was conducted during the period January to December 2014 in medical record department of Rajshahi Medical College and Hospital.

For assessing the management of medical record keeping purposively selected 160 discharged patients records were reviewed where there were total 6560 information focusing 9 important components of medical record and 20 respondents related to medical record management within the category of doctor, nurse and record keeper were interviewed using a check-list and an interview schedule. The collected data were processed and analyzed meticulously with the help of SPSS (Version 21) software on the basis of different variables. **Results:** The study result revealed that the information related to completeness of medical record, out of 6560 information, 86.2% was recorded and 13.7 % were not recorded. The respondents related to medical record management 60.0% were male and 40.0% were female and the age (mean±sd) was 41.7±7.0 years. About management status of medical record keeping respondents mentioned 90.0% follow coding system, 25.0% follow filing system, 80.0% properly maintained or documented medical record. **Conclusion:** Various problems were identified which could be minimizing by developing knowledge, skills and attitude towards the value of maintenance of medical records. Proper maintenance of medical record can provide better health care and assure the hospital quality service.

Key words: Record, Medical Record, Medical Record Management.

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Introduction:

The medical record is a multifunctional document that is used to communicate and document critical information about patients' medical care among health care professionals¹⁻⁴. Comprehensive medical records are a cornerstone in the quality and efficiency of patient care during the hospitalization and in subsequent follow-up

visits, as they can provide a complete and accurate chronology of treatments, patient results and future plans for care^{5,6}. Despite the importance of medical records to high quality and efficient care, management of medical records, particularly in developing countries, has not been a priority. Whereas in many high-income countries the medical records function is supported by extensive use of

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information technology,⁵⁻⁹ medical records in developing countries are generally inadequately supported and poorly managed. Although there are some exceptions with new open-source medical records systems becoming available,^{10,11} these are yet not widely used. In our country medical record management has not yet developed to the same extent as good as in developed countries. Since no organization can run perfectly without record, likewise medical record should be great interest to everybody working in the hospital. It may be unpleasant to state that many of our doctors, nurses and other concerned staff to not take adequate interest to maintain medical records. Moreover, they are neither being given any formal training for it nor any definite format has been developed in our hospitals. The aim of the study was to assess the different management aspect of medical record keeping such as the completeness of medical record with its important contents, medical record management status according to the statement of the respondents related to medical record management, the problems faced by the respondents during duty associated with the medical record management and to recommended for necessary improvement of medical record keeping practice in tertiary level government hospital of Bangladesh to improve better patient care.

Materials and Methods:

The descriptive type of cross sectional study was conducted in medical record department of Rajshahi Medical College and Hospital during the period January to December 2014. For assessing the management of medical record keeping purposively selected 160 discharged patients records were reviewed where there were total 6560 information focusing 9 important components of medical record and 20 respondents related to medical record management within the category of doctor, nurse and record keeper were interviewed using a check-list and an interview schedule. During data collection emphasis was given on checking of medical records by using the checklist to find out the completeness of medical record management. Then the master tabulation sheet was prepared after proper checking, verifying and editing as per specific objectives and key variables. Analysis of data was finally done with Statistical Package for Social Science (SPSS) software (version 21) of computer on the basis of difference variables. Then the data presentation was perfectly done by MS Word and MS Excel. Prior permission was taken from the concerned authorities. Verbal consent was taken from the respondents.

Confidentiality and anonymity of the respondents was maintained.

Results:

Table I: Distribution of the information according to completeness of medical record

Information related to completeness of medical record	Recorded n (%)	Not recorded n (%)	Total n (%)
Identification of data	2336 (85.8)	384 (14.1)	2720 (100.0)
Medical history	503 (78.5)	137 (21.4)	640 (100.0)
Laboratory report	142 (88.8)	18 (11.3)	160 (100.0)
Physical examination	551 (86.0)	89 (13.9)	640 (100.0)
Physician's order	567 (88.5)	73 (11.4)	640 (100.0)
Nurses record	400 (83.3)	80 (16.6)	480 (100.0)
Progress notes	284 (88.7)	36 (11.2)	320 (100.0)
Discharge notes	877 (91.3)	83 (8.6)	960 (100.0)
Total	5660 (86.2)	900 (13.7)	6560 (100.0)

Table I revealed that the combined result of completeness of medical record. Here, out of 6560 information regarding completeness of medical record 5660 (86.2 %) were recorded and 900 (13.7 %) were not recorded. In laboratory record, progress notes, physician's order, physical examination and medical history 88.8%, 88.7%, 88.5%, 86.0% and 78.5% information were recorded.

Table II: Socio demographic characteristics of the respondents related to medical record management

Age group (in years)	Frequency	Percentage
40	9	45.0
>40	11	55.0
Mean (\pm SD)	41.7 (\pm 7.0) years	
Category of the respondents	Frequency	Percentage
Doctor	9	45.0
Nurse	9	45.0
Record keeper	2	10.0
Training on medical record keeping	Frequency	Percentage
Have training	4	20.0
Don't have training	16	80.0

Table II revealed that the mean age of the respondents was 41.7 (\pm 7.0) years and the category of the respondents related to medical record management was 45.0 % were doctor, same percentages were nurse, 10.0% were record keeper. 80.0% respondents had not training, where as 20.0% had training on medical record management.

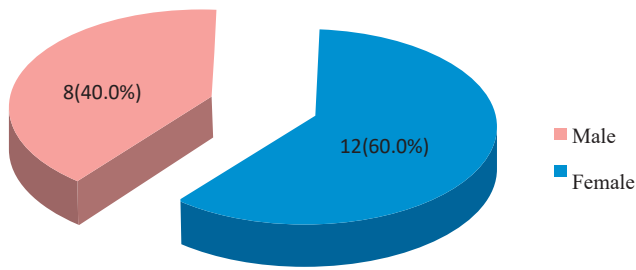
Figure 1: Distribution of the respondents according to sex (n=20)

Figure 1 shows 12 (60.0%) were male and 8 (40.0%) were female.

Table III: Distribution of the respondents related to medical record management according to their statement on medical record management status in the hospital.

Management status	Frequency	Percentage
Coding system for maintaining medical record:		
Follow coding system	11	90.0
Does not follow coding system	9	10.0
Filing system for maintaining medical record :		
Follow filing system	5	25.0
Does not follow filing system	15	75.0
Maintenance of medical record :		
Properly maintained or documented	16	80.0
Not properly maintained or documented	4	20.0
Supervision of medical record management by authority		
Regularly supervised	12	60.0
Not regularly supervised	8	40.0

Table III shows 90.0% mentioned coding system for maintenance of medical record is followed, 75.0% mentioned filing system does not follow, 80.0% mentioned medical record properly maintained or documented and 60.0% mentioned authority regularly supervise the medical record management in the hospital.

Table IV : Distribution of the respondents according to their suggestions for further improvement of medical record management system in the hospital.

Suggestions for further improvement of medical record management system	Frequency	Percentage
Adequate number of trained manpower should be increased	2	10.0
Compute based medical record keeping should be introduced	7	35.0
Both	11	55.0
Total	20	100.0

Table IV shows out of 20 respondents 55.0 % suggested to

increase adequate number of trained manpower and to introduced compute based medical record keeping for further improvement of medical record management system in the hospital.

Table V : Distribution of the respondents according to the problems faced by them during duty regarding medical record management.

Problems faced by respondents regarding medical record management	Frequency	Percentage
No problem	5	25.0
Lack of skilled manpower	11	55.0
Insufficient record room	4	20.0
Total	20	100.0

Table V shows out of 20 respondents 55.0 % mentioned about the problem lack of skilled manpower, 20.0% mentioned about insufficient record room and 25.0% did not face any problem during duty regarding medical record management in the hospital.

Discussion:

Medical record management has become an integral activity of the hospital management. A good medical record means good health care provided by the hospital authorities, doctors, nurses and other medical and non-medical personnel related to medical services. This study revealed that the information related to completeness of medical record, out of 6560 information, it was found that more than three fourth (86.2%) were recorded and less than one fourth (13.7 %) were not recorded (table I). According to Farhan et al. (2003)12 titled 'Documentation and coding of medical records in a tertiary care center: a pilot study' out of 1051 items abstracted, 876 (83.3%) were accurately documented, 41(3.9%) were inaccurately documented and 134 (12.7%) were not documented, which was quite consistent with this study findings. The study findings also reveals the mean age of the personnel related to medical record management was 41.7 ± 7.0 years (table II), among the respondents more than half (60.0%) were male and 40.0 % were female (figure 1), with the category of 45.0 % doctor, 45.0 % nurse and 10.0 % record keeper, among them 80.0% respondents had not training, where as 20.0% had training on medical record management (table II). One fourth of the respondents (25.0%) mentioned they follow filing system where as three fourth (75.0%) of the respondents mentioned that they do not follow filing system.

Majority of the respondents (90.0%) mentioned that they follow coding system for maintaining medical record (table 3). According to Farhan et al. (2003) 12 out of 1051 abstracted items, 736 (70%) were assigned a correct code, 110 (10.5%) were assigned an incorrect code and 205 (19.5%) were not coded, which was close with the study finding. More than three fourth (80.0%) mentioned medical record are properly maintained in the hospital, where as 20.0 % mentioned medical record are not maintained properly (table III). More than half of the respondents (60.0%) mentioned authority regularly supervised the management of medical record (table III). More than half (55.0%) suggested to increase adequate number of trained manpower and to introduced compute based medical record keeping for further improvement of medical record management system in the hospital (table IV); and about the problem lack of skilled manpower, insufficient record room mentioned by 55.0% and 20.0% respondents respectively (table V). A well organized medical record management system can be effective in improving patients information accessibility and completeness in hospital both in developing and low income countries despite the lack of resources. Longer follow up is required to assess the sustainability of the hospital improvements accomplished.

Conclusion:

Based on the findings of the present study, it is evident that most of the information was recorded. Only in a few cases the information were not recorded. Though the information were mostly recorded there were problems associated with medical record maintenance mentioned by the respondents related to medical record management where attention should be paid by hospital administrators. About management status it was observed most of the respondents follow coding system, but majority do not follow the filing system, majority properly maintained or documented medical record. Without proper medical record management, medical audit will be impossible, which is the primary requirement for quality assurance programme and prerequisite for quality medical service. Focusing the suggestions of the respondents it is necessary to ensure regular supervision by higher authority as well as adequate professionally trained record personnel for proper assembling, coding, indexing, tiling and retrieval of medical record for better management.

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A Vitro Study on Fracture Resistance of Fiber Reinforced Composite Post System

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Abstract:

Background: Grossly carious teeth with broken down crown are needed to be restored with post & core after endodontic treatment. Root canal posts are widely used & come in a variety of metals & forms. However, cast metal posts, although better than other post & core systems, still possess some disadvantages. **Purpose:** The purpose of this study was to investigate the success of fiber reinforced composite post & core system over conventional metallic system in regards of fractures resistance. **Materials & Methods:** This was a prospective study, conducted in the department of Conservative Dentistry & Endodontics, BSMMU. Total 30 caries free human maxillary single rooted anterior teeth were examined in this study. Thirty teeth were tested for fracture resistance under universal testing machine. The recorded data were compiled on a master chart & statistically analyzed. Chi-square test & t-test (unpaired) were done for statistical significance ($p < 0.05$). **Results:** Insignificant difference ($p > 0.05$) was observed in fracture resistance test. **Conclusion:** Fiber reinforced composite post system has lesser chance of root fracture.

Key words: Dowel crown, Fiber reinforced composite post, Fracture resistance.

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Introduction:

Longevity of a tooth restored with dowel crown depends on retention of post, resistance of root fracture and development of any apical lesion due to any micro leakage. All these criteria for good prognosis can be achieved by selecting a proper design of post with employing correct geometry and extension of ferrule. So, an appropriate post design is very essential for longevity of a tooth restored with dowel crown¹. A post is commonly placed in an attempt to strengthen the tooth. However, dentin must be removed during preparation of the post hole and the consequent reduction in fracture resistance may outweigh any likely gains. The post does not actually strengthen the root, but rather serves to improve retention of the core²⁻⁵. Prior to begin the clinical procedure for a single crown or fixed partial denture, some important characteristics should be assessed for the fabrication of a post & core. One of these characteristics is the selection of the type of posts. Different types of available procedures for dowel

fabrication are followed worldwide but not all the procedures ensure sound and prolong prognosis of a dowel crown with good retention and stability. Recently, posts made of fiber reinforced composite polymers (Ribbond, Fiberkor Post System, Composipost, Snow Post System) have been introduced. Esthetic version of these posts has a quartz exterior that makes the post tooth colored. Fiber reinforced posts are made of a woven polyethylene fiber system, that is coated with dentin bonding agent & packed into the canal, where it is then light polymerized in position⁶. Differences of opinions exist regarding effectiveness of post design. According to STAINBUSTER- the member of the Industrial Diamond association, the ideal post material & the associated core composite material should be similar, thus permitting a homogenous reconstruction on a mechanical as well as a chemical point of view⁷. According to their discussion, there are some criteria that are expected of the ideal root post.

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"First of all, it should not further weaken a tooth that has already been endodontically treated. Instead, it should allow a reconstitution while preserving a maximum of healthy dentin. Secondly, the tooth reconstitution should have an elasticity modulus close to that of the dentin, which ultimately reduces the chances of fracture of the post & increase the retention. The ideal post should permit a quick, simple & affordable procedure. The post should also be bio-compatible, radio-opaque & easy to remove if necessary. Finally, the color of the post should adapt to the demands of esthetic dentistry⁸. Research indicates that fiber reinforced posts possesses adequate rigidity,⁹ are not prone to produce tooth fracture,^{10,11} & have shown to be clinically successful¹². Composipost systems are passive & are designed to be used with a bonding technique. The recommended core material is resilient composite, a BIS-GMA resin filled with short glass fibers. According to the manufacturer, the tensile strength of the Composipost dowel is 1600 MPa. It has been suggested that a post should have a modulus of elasticity similar to dentin for more uniform distribution of forces along the length of the post. In a recent study of stored Composipost dowels, reported values of flexural modulus & ultimate flexural strength are 82 ± 6 CPa & 1154 ± 65 MPa, respectively^{13,14}. The use of fiber reinforced composite as post material for prefabricated posts offers a number of advantages, including biocompatibility, resistance to corrosion and fatigue, mechanical properties that closely match those of the tooth,^{15,16} and the option of easy removal of the post from the root canal^{17,18}. Once cemented, metal posts are considerably more difficult to remove. Therefore as the fiber reinforced composite post system is an established post system, our study has been designed to examine its modulus of elasticity and fracture resistance in vitro to evaluate the efficiency of fiber reinforced composite post system.

Methodology:

After collection of the teeth all the teeth were immersed in 5.25% NaOCl solution in a screw capped glass vial for overnight before being stored in a 0.9% normal saline solution until use. Before storing all the teeth were cleaned carefully with hand and ultrasonic scaler to remove calculus tarter stain and remained organic tissue debris. Clinical crown was sectioned at the cemento enamel Junction with a low speed diamond saw under continuous water spray.

Root canal was prepared using protaper (protaper universal/densply) system and the working length was 1mm

short of the apex. Apical patency was be maintained with 15 K file 5.25% NaOCl and Glyde was used throughout the instrumentation phase for irrigation and lubrication respectively. After cleaning and shaping the canal was dried with paper point and obturated with GP (Gutta Percha Auxillary Point/Densply) and sealer. After obturation a radiograph was taken to check the quality and length of obturation.

A 9 mm post space was made in each root canal with a drill (GGB, Pesso Reamer & Luminex drill respectively). The smear layer was removed from the canal wall by 1 minute application of 17% EDTA followed by a saline rinse and 1 minute application of 5.25% NaOCl, also followed by a saline rinse. The canal was dried with paper point, conditioning the canal with conditioner (NRCTM/DENTSPLY) with a brush and leave undisturbed for 20 seconds, then apply one layer of bonding (Prime & Bond NT/DENTSPLY) with a disposable brush and blowing with gentle air from a dental syringe for at least 5 sec to remove excess bonding. Leave the surface undisturbed for 20 sec. When the surface become glossy and smooth apply light for 10 seconds.

Luting cement (Dyract® Cemplus/Densply) was mixed and apply over post (Dentatus Classic post system/Densply) with a brush and inserted in to canal up to its full length and apply light from the top of the post for 10 sec (Selector - L). Composite core were build up over the post for fracture resistance test after etched the surface 20 sec with 37% orthophosphoric acid, washed with water spray for another 30 sec and dried the etched surface by air blow. The post and tooth surface were coated with bonding agent & applied halogen light for 10 seconds. Now apply composite incrementally around the post and dentin. Each increment was packed and cured with halogen light for 20 sec. After placing the final increment light was given for 40 sec. Now a definite crown preparation was done with diamond bar. The specimens were then thermo cycled at $5-55^{\circ}$ C for 1200 cycles, lasting 30 secs at each temperature.

After preparation each tooth was mounted in metallic tray with die stone at a depth 2mm bellow the cemento-enamel junction for fracture resistance test. After setting a custom made metallic sample holder were used to position the specimen in the universal testing machine so that the load were directed 450 angle. Samples were loaded at a rate of 0.5 mm/min until failure occurred. The force causing fracture was recorded.

Results & Observations

Thirty recently extracted caries free human maxillary single rooted anterior teeth were included in this study. Twenty teeth were designated as study group and 10 teeth as control. The observed results were used to compare the results in groups. Force causing tooth fracture was recorded for fracture resistance test.

Table I: Comparison of fracture resistance between study & control

Grouping of the Study subjects	Resistance transfer In lb	t - value	p value
Study (n = 20)	234.27 ± 2.1	- 1.864	> 0.05
Control (n = 10)	235.75 ± 1.92		

Resistance of fracture shown in table I, was evaluated by chi-square test & the P-value was >0.05 which is not significant.

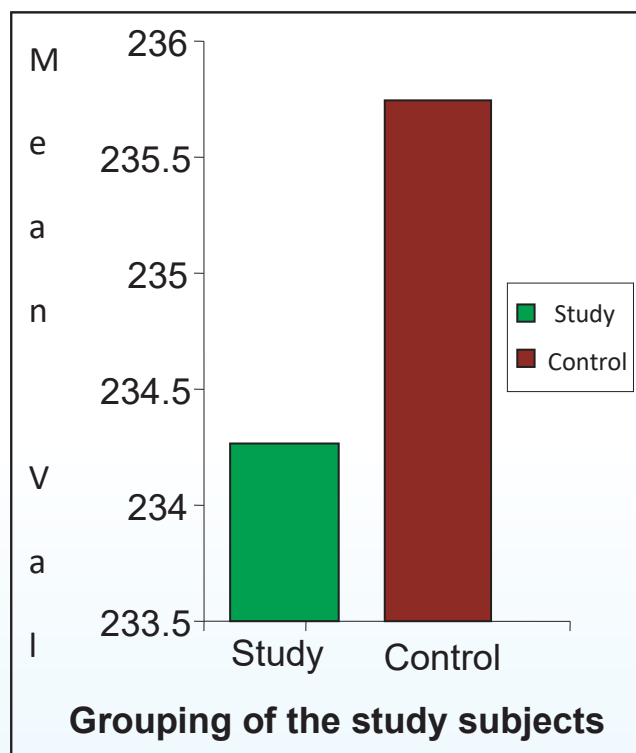


Fig 1: Comparison of fracture resistance between study & control

Resistance of fracture shown in figure 1, was evaluated by chi-square test & the P-value was >0.05 which is not significant.

Discussion:

According to Lui (1999), 'Badly broken down pulpless teeth usually need root retained restorations. Endodontically treated teeth are not strengthened by the placement of the posts, but retention of the restoration is enhanced by the use of a post. It is thought that filling the post space with a new generation of composites and dentin bonding agents may produce superior adaptation to the dentinal walls²².

In this study, only 1 (5%) of 20 teeth restored with fiber reinforced composite post system was failed due to lack of adhesion between the dentin, core material and post. According to Purton and Payne (1996) one of the main failure reasons with fiber post is the lack of adhesion between the core material and the post²³.

Lacy (1995) and freedman (1996) narrated that to choose an ideal post material; the modulus of elasticity is of a prime factor. If the modulus of elasticity of post material is nearer to dentin, more uniform distribution of forces along the length of tooth is ensured. As a result chance of root fracture becomes lesser²⁴.

Composite posts has additional shock absorbing effect of the resin matrix and the thickness of the adhesive cement used for sealing the post, as a result the stress is transmitted progressively and regularly to all the coated surface (Abrasive Technology Inc. 2004). The use of fiber post for restoring endodontically treated teeth has increased because of the reduced risk of fracture, since their modulus of elasticity is similar to that of dentin^{25,26}.

Conclusion:

In this vitro study, following conclusion were drawn

- The fracture resistance offered by the FRC post system was nearer to the fracture resistance offered by the natural teeth.
- Therefore the modulus of elasticity of this post system can be said to be very near to the dentin. As a result of that, the chance of root fracture is less if this system is used to restore the broken down teeth.

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A Study on Arch Widths of Bangladeshi Adult Subjects with Class II-2 Malocclusion Compared to Those with Class II -1

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Abstract:

Aim: To evaluate the transverse discrepancy in Class II div 1 malocclusion and class II div 2 malocclusions. Also to test the hypothesis that models with class II div 2 malocclusions may have mean maxillary arch widths significantly larger than those with class II division 1 malocclusion. Thus the proposed study will generate interest among the orthodontists for further study over the transverse discrepancy of our patients and guide them to establish effective treatment strategy and their management. **Materials and Methods:** Cross sectional comparative study was carried out Department of Orthodontics & Dentofacial Orthopedics of Dhaka Dental College & Hospital; Dhaka with 100 samples was included in this study. **Results:** Maxillary intercanine, interfirst premolar and interfirst molar widths between Class II div 1 malocclusion and class II div 2 malocclusions were statistically significant. Maxillary measurements of class II div 1 malocclusion occlusion were smaller than Class II div-2 malocclusion. Mandibular intercanine, interfirst premolar and interfirst molar widths between Class II div 1 malocclusion and class II div 2 malocclusions were statistically significant. **Conclusion:** This study helps in determining possible differences in the dental arche widths of Bangladeshi people in Class II-2 adults compared to adults with class II-1 may be an important aid in further understanding of dentoalveolar characteristics of these conditions, as well as improving their management.

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Introduction:

Clinicians speculate that nasal obstruction, digit habit, tongue thrusting, low tongue position, abnormal swallowing and sucking habit are the reasons for narrow maxillary dental arch width in class II Division 1 malocclusion¹. Class II malocclusion is a common type of malocclusion that may present a variety of skeletal and dental configurations^{2,3}. Maxillary protrusion and mandibular retrusion is a frequent dentofacial anomaly in various populations⁴. Skeletal class II patterns arise from not only sagittal, but also from vertical discrepancies⁵. Dental class II malocclusion presents with distal relationship of lower teeth to upper and further has two divisions; Class II division 1, and class II division 2.6 In an effort to describe the typical class II division 1 malocclusion, the following are the characteristics¹⁵. In frontal view face is usually oval (Mesocephalic to Dolicocephalic). A convex profile with

posterior divergent face, Incompetent or stretched upper lip due to proclined upper incisors, Lower lip is everted and there is lack of lip seal. Intra orally Class II molar relationship, proclined upper incisors and an increased overjet. An exaggerated curve of spee of mandible, Upper arch is usually narrow, V shaped. There is deep bite which is usually traumatic in nature. Other features may be an open bite, cross bite, crowding etc. Staley et al. started that maxillary dental arch width of Class II Division 1 is narrower as compared to maxillary dental arch width of normal occlusion samples. According to the result for maxillary arch; the statistically significant difference among the group were found in the maxillary inter-premolar width. In Bangladesh, no studies been conducted except Rahman (2007)¹⁶ and Islam (2011)¹⁷. Till now, our efforts were confined to isolated case management and study the

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prevalence of different malocclusions. A definite study in determining possible differences in the dental arches widths of Bangladeshi people in class II-2 adults compared to adults with class II-1 may be an important aid in further understanding of dentoalveolar characteristics of these conditions, as well as improving their management.

Methods:

The cross sectional study was carried out Department of Orthodontics & Dentofacial Orthopedics of Dhaka Dental College & Hospital, Dhaka. In this study 100 pair of study models was selected from patients and students of the Orthodontics & Dentofacial Orthopedics Department of Dhaka Dental College & Hospital and were divided into two groups. The first group consisted of 50 pairs of dental casts with permanent dentition and diagnosed as class II division-2 malocclusion. The second group includes another 50 pairs of dental casts with permanent dentition and diagnosed as class II division 1 malocclusion. This group of malocclusion was again subdivided into two categories, class II division-2 malocclusion with crowding and class II division-2 malocclusion without crowding.

Dental cast's measurement was performed by a digital slide caliper to the nearest 0.01mm. All measurements of all subjects were carried out again two weeks later by another operator to evaluate measurements error. Almost all the measurements were same measured by two operators, where differed, average was taken. After collection of data, the obtained data was checked, verified. These were entered in a personal computer using the SPSS (statistical package for social science) software. Entered data were cleaned, edited and appropriate statistical tests were done depending on the distribution of data.

Data were analyzed through standard statistical methods by using SPSS software. Version 19.0 (statistical package for social science SPSS Inc. Chicago, USA) statistical software employing appropriate statistical tests definite unpaired Student's "t" test, mean, SD, 95% Confidence Limit, Standard Error and their "p" values were obtained to see the statistical significance. P value < 0.05 was considered as significant.

Inclusion criteria: For class II division 1 malocclusion (50 subjects)

1. Bilateral class II molar relationship.
2. Protruded maxillary incisors ,overjet more than 5 mm.
3. Convex soft tissue profile.

4. No missing teeth, except wisdom teeth.
5. Absence of posterior crossbite.
6. No history of previous orthodontic treatment.

Exclusion criteria:

1. Posterior crossbite
2. Missing teeth other than wisdom teeth.
3. Age below 13 years.
4. History of previous orthodontic treatment.

Results:

Table shows maxillary intercanine, interfirst premolar and interfirst molar widths between Class II div 1 malocclusion and class II div 2 malocclusions were statistically significant. Maxillary measurements of class II div 1 malocclusion occlusion were smaller than Class II div 2 malocclusion (table-1). In current study showed mandibular intercanine, interfirst premolar and interfirst molar widths between Class II div 1 malocclusion and class II div 2 malocclusions were statistically significant. mandibular measurement of class II div 1 malocclusion were smaller than Class II div 2 malocclusion (table-2).

Table-I: Comparison of maxillary measurement between Class II div 1 malocclusion and class-II div-2 malocclusions

	Class II div 1 maloccl usion (n=50)	Class II div 2 malocclu sion (n=50)	P value
	Mean (mm) (±SD)	Mean (mm) (±SD)	
Mandibular intercanine width	24.48 (±1.70)	25.97 (±1.88)	<0.001*
Mandibular interfirst premolar width	32.75 (±2.10)	34.32 (±2.56)	0.001*
Mandibular interfirst molar width	42.45 (±2.63)	44.68 (±2.05)	<0.001*

Level of p value significant = <0.05.

Table-II: Comparison of mandibular measurement between Class II div 1 and class-II div-2 malocclusions.

	Class II div 1 malocclusion (n=50)	Class II div 2 malocclusion (n=50)	P value
	Mean(mm) (±SD)	Mean(mm) (±SD)	
Maxillary intercanine width	32.04 (±2.43)	34.10 (±2.08)	<0.001
Maxillary interfirst premolar width	38.27 (±2.56)	39.85 (±2.73)	0.004
Maxillary interfirst molar width	48.18 (±2.50)	50.33 (±2.05)	<0.001

Discussion

In Bangladesh the incidence of Angle's Class II div 1 malocclusion is 32.74% and 28.86%^{8,9}. The report suggests that the incidence of such class II division 1 highest among the malocclusion groups. Today literature in this field, in context to our country has been very inadequate. A few dissertation works have been done previously which is related to this study in the department of Orthodontics & Dentofacial Orthopedics of Dhaka Dental College and Hospital. Thus the proposed study will generate interest among the orthodontists for further study over the transverse discrepancy of our patients and guide them to establish effective treatment strategy and their management. In our study to compare arch widths, we selected subjects without posterior crossbite, even in a single tooth. This will ensure accurate measurements of arch widths and will not affect the result. In addition to measurements in canine and molar region, arch widths between premolar teeth were also calculated. In this study found maxillary intercanine, interfirst premolar and interfirst molar widths between class II div 1 and class II div 2 were statistically significant. Class II div 2 were greater than class II div 1 malocclusion (Table-1). In comparison of maxillary measurements between normal occlusion, class I crowded and class III malocclusion among males and females, it was found that class I crowded male had significantly larger inter-premolar, inter-molar and alveolar width. In class III malocclusion, males had a significantly larger inter-canine and alveolar width than the females¹⁰.

In this study shows mandibular intercanine, interfirst premolar and interfirst molar widths between class II div 1 and class II div 2 were statistically significant. Class II div 2 were greater than class II div 1 malocclusion (table-2). In the mandible, it was revealed that males had a significantly larger inter-molar and alveolar arch width than the females in all three groups. Comparison of maxillary and mandibular measurements within the all class groups, among the males, it was revealed that the maxillary and mandibular inter-molar width were significantly smaller in class I crowded males¹¹. In another Bishara et al.¹² and Frohlich¹³ study was showed that found no difference in interfirst molar widths between Class I normal occlusion and Class II subjects. Dhaka¹¹ showed constriction of the mandibular inter-canine distance in class II Division 2 subjects. It is suggested that Class II Division 2 malocclusion is characterized by normal transverse dimensions in the maxillary and mandibular posterior segment but reduced inter-canine arch dimension in the mandible¹⁴. The finding might be in a specific area which may not represent the whole national situation. The study was not done in a specific race of population. The size of the sample of the study was very small to represent the situation prevailing the nationality.

Conclusions:

According to the results of this study in conclusion followings are reached: Subjects with class II division 2 had mean maxillary mandibular intercanine, interfirst premolar and interfirst molar widths larger than Class II division 1 malocclusion. Mandibular intercanine inter first premolar and interfirst molar widths were larger class II div 2 than class II div 1. Subjects with class II div 1 had mean maxillary intercanine, interfirst premolar and interfirst molar widths smaller than Class II division 2 malocclusion. All groups of maxillary arch width have significantly larger arch width than mandibular arch width.

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Role of Sclerotherapy in Trigeminal neuralgia

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Abstract:

Background: Trigeminal Neuralgia (TN), often called "tic douloureux," is one of the most painful and debilitating pain disorders. Trigeminal neuralgia, characterized by paroxysms of severe, lancinating, "electric-like" bouts of pain, is almost exclusively, unilateral, solely within the distribution of the trigeminal nerve, typically with tactile triggers, and without a neurosensory deficit. **Objective:** To assess the efficacy of Sclerotherapy in Trigeminal neuralgia and to compare this procedure with Carbamazepine and Ethyl alcohol. **Materials and method:** A prospective study with 50 cases of Trigeminal neuralgia was carried out in the Department of Oral and Maxillofacial Surgery, Rangpur Dental College from January 2014 to December 2015. Out of 50 cases 25 received Carbamazepine and 25 received alcohol block. Visual linear analogue scale (VAS) was used to measure pain intensity in different groups. **Results:** Out of different treatment modalities on follow up onwards pain control was better in alcohol block than Carbamazepine. **Conclusion:** Trigeminal neuralgia remains a difficult condition to treat and can be managed both medically and surgically. This study reveals that the efficacy of alcohol block is superior to Carbamazepine to eliminate the pain intensity in Trigeminal neuralgia.

Key words: Trigeminal Neuralgia, Cryosurgery, Alcohol block, Carbamazepine.

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Introduction:

Trigeminal Neuralgia (TN), often called "tic douloureux," is one of the most painful and debilitating pain disorders. Trigeminal neuralgia, characterized by paroxysms of severe, lancinating, "electric-like" bouts of pain, is almost exclusively, unilateral, solely within the distribution of the trigeminal nerve, typically with tactile triggers, and without a neurosensory deficit. It is either idiopathic due to a structural lesion involving the trigeminal system, or associated with some other neurological process. Presentation of neurogenic facial pain may be somewhat atypical in some patients. This atypical facial pain (AFP) may start out as a diffused, poorly localized pain, which is described as dull, aching, burning, throbbing or crawling in nature¹.

Currently, clinical cases of TN fall into two groups: "classical" (primary) and "symptomatic" (secondary) forms of TN. Classical TN refer to the "idiopathic" syndrome, meaning that the underlying cause of the disorder is not

known. Over 90% of TN patients fall into this category. Symptomatic TN identifies a group of patients that exhibit the clinical syndrome of TN as a symptom of another disease process. The most common disorder associated with symptomatic TN is multiple sclerosis and benign tumors of the Gasserian ganglion, trigeminal root, or cerebellopontine angle. The diagnosis of TN is based primarily on a clinical history consistent with the diagnostic criteria. However, general physical and neurological examinations are also very important. Imaging may prove valuable when the clinical presentation does not match the classic diagnostic criteria. Most can be identified by a careful medical history; physical examination and magnetic resonance imaging (MRI) usually reveal more specific and different findings². At present it is a standard practice to use carbamazepine as the first line of treatment, sometimes with the later addition of phenytoin. Even though many patients can be managed in the long term by carbamazepine, side effects become intolerant and quite a number of patients become intolerant

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and resistant to the drug and required a variety of surgical procedures. In order to avoid major surgery, numerous peripheral techniques have been used. These have included peripheral neurectomy, alcohol or phenol injections, peripheral radiofrequency thermolysis and peripheral streptomycin and Lidocaine injection. None of the technique appears to be curative and some may cause complications such as neuromas, anaesthesia dolorosa and neurological deficits. The use of cryotherapy was first reported since 1976 with encouraging results. They treated 64 patients suffering from intractable pain, six of whom had "facial pain" cyrotherapy was used in variety of facial pains, including post herpetic neuralgia atypical pain and paroxysmal trigeminal neuralgia. They found that only the last named group really benefited from³.

Sclerotherapy is a method of local destruction of tissue by injecting more than 95% absolute Ethyl Alcohol. Tissue death results from a combination of direct cellular effects, such as cellular dehydration, protein denaturation and disruption of cell membranes and from ischemic infarction resulting from failure of the microcirculation. Vascular stasis enhances the direct lethal effect⁴.

A sclero lesion will produce a second-degree nerve injury (Degeneration of axon, but endoneurium, perineurium and epineurium remains intact) with complete degeneration distal to the lesion (wallerian degeneration). The effect is reversible however, and recovery occurs in 42 days with a remarkable absence of fibrosis and scar formation. The schlerolesion will result in selective nerve-fiber destruction; the fibers that are most vulnerable are pain fibers, since they are of a smaller diameter than the majority of fibers on a mixed peripheral nerve⁵.

Many clinically diagnosed patients with trigeminal neuralgia visit this Hospital who was resistant to carbamazepine therapy. Among the different treatment modalities sclerotherapy may be one of the good options of peripheral surgical technique for the treatment of trigeminal neuralgia. Thus this study is conducted to evaluate the real efficacy of sclerotherapy in the treatment of trigeminal neuralgia.

Materials And Methods:

A prospective study with 50 cases of trigeminal neuralgia was carried out in the Department of Oral and Maxillofacial Surgery, Rangpur Dental College from January 2014 to December 2015. Out of 50 cases 25 received Carbamazepine and 25 received alcohol block. Visual linear

analogue scale (VAS) was used to measure the pain intensity in different groups. Patients were selected purposively irrespective of age and sex with considering diagnostic criteria.

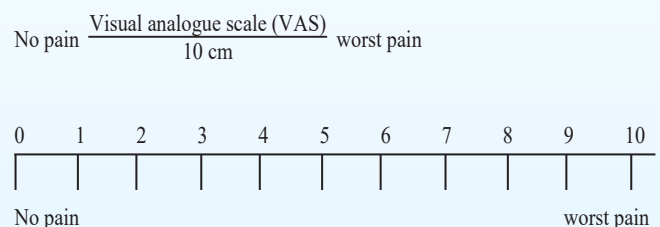
Diagnostic Criteria: Pain in the distribution of trigeminal nerve, Pain of electric shock, shooting or stabbing in character of short duration and showing refractory periods, Presence of trigger zones, Proxysmal pain with episodes of complete remission, Pain provoked by innocuous stimuli, Complete abolition of pain by LA injection into the trigger zone or by regional block and diagnostic trial of carbamazepine.

Group-I: The group treated by pharmacological therapy (Carbamazepine); Drug category: Anticonvulsants-Carbamazepine (Tegretol). The starting dose is usually 100mg twice a day with increment of 100mg daily every third day up to 800 mg/day and continued.

Group-II: The group treated by alcohol nerve block; Types of alcohol: Absolute alcohol (95% ethyl alcohol).

Method of application: After standard preparation with povidone iodine at first 1ml of lignocaine with 1 in 80,000 adrenaline was given into the trigger area and the pain relief was monitored. If the pain was abolished, 0.5ml-1ml of absolute alcohol was injected using an aspiration technique into the peripheral branch of trigeminal nerve. The date of first injection and last date to follow up were noted. Maintenance dose of carbamazepine was 200 mg b.d.

Pain Assessment: VAS consist of 10 cm horizontal line with two end points labeled as no pain and worst pain ever. The patient is required to place a mark on the 10 cm line at a point which corresponds to the level of pain intensity he/she presently feels. The distance in centimeters from the lower end of the VAS to the patients mark is used as numerical index of the severity of pain. Ask the patient to indicate on the line where pain is in relation to the two extremes i.e. a midpoint mark would indicate that the pain is approximately half of the worst possible pain. Intensity of pain among the group was assessed by the level of pain reduction in different visits.



Results:

A total of 50 patients involving 20% Inferior alveolar, 22.7% Inferior alveolar and mental, 42.7% Infraorbital, 13.3% mental and 1.3% Infraorbital and mental were divided in three equal groups and pain Intensity in different visits were measured by visual linear analogue scale (VAS).

Table I: Distribution of the patients according to intensity of pain in different visits

Visit	Treatment			
	Group I n=25		Group II n=25	
	n	%	n	%
1st visit				
Pain free	0	.0	0	.0
Mild	1	4.0	4	16.0
Moderate	13	52.0	17	68.0
Severe	11	44.0	4	16.0
2nd visit				
Pain free	0	.0	0	.0
Mild	0	.0	1	4.0
Moderate	16	64.0	22	88.0
Severe	9	36.0	2	8.0
3rd visit				
Pain free	0	.0	0	.0
Mild	0	.0	2	8.0
Moderate	17	68.0	22	88.0
Severe	8	32.0	1	4.0

Table II: Mean score of pain in different visit among the different treatment group

Visit	Mean pain score (SD)		
	Group I n=25	Group II n=25	p value
Base	100.0	100.0	-
1 st visit	64.0±17.3	49.6±13.7	0.001
2 nd visit	62.0±13.2	52.4±10.1	0.001
3 rd visit	60.0±11.2	49.2±10.8	0.001
p value	Base vs. 1 st visit (p<0.001)	Base vs. 1 st visit (p<0.001)	
	1 st vs. 2 nd (p>0.05)	1 st vs. 2 nd (p>0.05)	
	2 nd vs. 3 rd (p>0.05)	2 nd vs. 3 rd (p>0.05)	

p value reached from repeated measure student's "t" test

p value reached from repeated measure ANOVA

Group I= Carbamazepine

Group II= Alcohol block

Table I showed that patients treated with carbamazepine there was no patients who become pain free in 3rd visit. However, 17 68.0 had moderate and 8 32.0 had severe pain. On the contrary patients with treated with alcohol 16 64.0 of the patients become pain free at the 3rd visit and only 9 36.0 had mild pain. No moderate or severe pain was reported among the patients treated by alcohol block. This shows that alcohol block was more effective for the treatment of TN than carbamazepine.

In table II One way analysis of variance indicated that among the different treatment groups a statistically significant mean difference of pain score was found in different visit $p<0.001$. However, within the group, repeated measure analysis of variance indicated that in group I patients a statistically significant mean score of pain decreased in 1st visit, but from 1st and subsequent visits no statistically significant pain decrease $p>0.05$. On the contrary, among the group II patients, the pain score decreased in from baseline to 1st and subsequent visits $p<0.001$. This indicated that the sclerotherapy was more effective in reducing the pain intensity.

Discussion:

A number of different peripheral surgical techniques such as cryosurgery, alcohol block, and selective neurectomy have been suggested for the management of trigeminal neuralgia all of which broadly aim to interfere with afferent pathways from the trigger zone to prevent stimulation of aberrant conduction pathways. Injections of alcohol have been suggested in the management of trigeminal neuralgia since the early 20th century. Alcohol injection have been widely used both at the level of the Gasserian ganglion and more peripherally.

The mean age of the patient was 51.6±8.8 years in group I, 47.8±12.4 years in group II and 51.3±11.7. The mean years of duration of pain were 3.6±2.7 years, ranging from 1-15 years. In case of type of nerve involvement 42.7% had infraorbital nerve, 22.7% had inferior alveolar and mental nerve, 20% of the had inferior alveolar nerve, 13.3% patient had mental nerve and 1.3% of the patient had infraorbital and mental and mental nerves but there is no involvement of ophthalmic division of trigeminal nerve. In this study baseline statistics like age, sex, and duration of pain, nature of pain, site and type of nerve involvement was more or less similar with the previous studies.

Similar study showed by Blom in 1962 was a major breakthrough and it has become accepted as first line management Al-Ubaidy and Nally (1976) found it initially effective in 84% of patients. Taylor et al. (1981) reported it effective in 69% of patients falling to 56% in the long term. However, Bradley et al. (2004) shows carbamazepine is the most effective drug for the treatment of trigeminal neuralgia, at the condition responds in approximately 75% of the patients. In this study pain reduction in different follow up visits ranges from 36-40%. On the contrary pain reduction was higher in previous study which ranges from 56-84%. These differences of pain reduction with previous study may be due to drug resistance because most of the patients in this study were taken carbamazepine previously^{9,10}.

Similar study shows the length of total pain control period for those having an alcohol injection varied from one month to three years with median time of 13 months for the first alcohol block. The median time to recurrence is i.e. probability of 50% getting a recurrence. However McLeod et al., 2007 reported the effect of peripheral alcohol injections ranges from 6 months to 24 months, with some variation in the results obtained from the different peripheral branches. In this study, pain reduction in different visits ranges from 47.6-50% with some negligible complication like truisms and swelling. But in previous studies pain control period ranges from 6 months to 14 months with some variation in different peripheral branches. This may be due to their longer duration of follow up and repeated alcohol nerve block^{5,11}.

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Total Count of Red Blood Cell, Packed Cell Volume (PCV) Status in Rural and Urban Women of Reproductive Life

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Abstract:

Background: The women are the poorest at the rural areas of Bangladesh. They have few earning opportunities in the community. As a result, their nutritional intake is often inadequate. They also poorly informed about their physical wellbeing of health and bodies. Most of them have incomplete knowledge, and are confused about their reproductive life. **Objectives:** To observe red blood cell count and packed cell volume in rural and urban women of reproductive age. **Methods:** This cross sectional study was conducted in the outpatient department of model family planning clinic of Rangpur Medical College, Rangpur from July 2012 to June 2013. A total number of 100 women of reproductive aged 18-45 years were selected, among them 50 were healthy urban women (Group A) and 50 were rural women (group-B). Blood was collected from each subject to detect red blood cell that was measured by DC detection method. Packed cell volume (PCV) was measured by cumulative pulse height detection method. For statistical analysis, independent sample 't' test was performed by using SPSS 15.0 versions for windows. **Results:** RBC and PCV were decreased ($p < 0.05$, $p < 0.001$ respectively) in rural women than that of control group. **Conclusion:** Red blood cell and packed cell volume were decreased in rural women than urban women of reproductive age.

Key words: RBC, PCV, Rural & Urban women.

Rangpur Dent. Coll J 2017; 5(2): 28-31

Introduction:

In an area of 145,000 square-kilometers Bangladesh is one of the most densely populated countries in the world. There are nearly 861 people live in per square kilometer. Most of them are living in the rural areas. Among them women are the poorest at the remote areas because of lack of services such as education and health care. They were suffering from discrimination, few earning opportunities and their nutritional status is very low¹. They got married at an early age (18-19 years) and almost immediately become adolescent mother, about 57% by the age of 18 years².

Poverty and nutrition are closely related. Poverty leads to hunger, ill health and undernutrition³. Poor socioeconomic condition associated with a number of factors such as high parity, short birth interval, poor diet both in quantity and quality, lack of health care and nutritional awareness leads to maternal undernutrition⁴. Under nutrition is especially

critical for women because inadequate nutrition causes not only havoc to her own health but also that of their children. Maternal malnutrition during pregnancy increases the risk of mortality, as well as it affects fetal growth, resulting in low birth weight, risking the survival of the child. They do not maintain the standard of sanitation and hygiene habits. They have also lack of knowledge about standard of living status³. Parasitic infestation is one of the most common problems in rural people of Bangladesh. The hookworm excites to the villi for continuous bleeding. Hookworm infestation and under nutrition causes anemia in rural people of Bangladesh⁵. Anemia is a wide spread public health problem associated with an increased risk of morbidity and mortality especially in rural women⁶. Iron deficiency anemia is one of the most common nutritional disorders and it has public health importance in developing countries like Bangladesh. Nutritional anemia is the common in adolescents and women of reproductive age,

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especially in rural area because of their more iron demand⁷. During this period owing to iron loss from menstruation and less intake of iron containing diets. All of these factors decreased red blood cell count and packed cell volume (PCV) in rural women of reproductive life⁸. The effects of low RBC and PCV status remain largely unexplored⁹. Maternal iron deficiency causes adverse pregnancy outcomes, impaired immune responses, gastrointestinal abnormalities, changes in the hair and nails, impaired thermogenesis, altered thyroid metabolism and changes in catecholamine turnover. In the urban areas about 37% populations are living below national poverty line⁴. Though, they maintain a better standard of living status than rural people. They try to maintain better nutritional requirement, sanitation and hygiene habit³.

Materials and Methods:

This Cross-sectional analytical study was carried out between July 2012 to June 2013 in Model Family Planning Clinic of Rangpur Medical College & Hospital, from the rural and urban women of reproductive age were 18-45 years. Study was done on a total number of 100 subjects, who were divided in two following groups, apparently 50 healthy subject were selected from rural area as experimental group. Age matched apparently 50 healthy subjects were selected from the urban community as control group. Sampling method was purposive.

After selection of subjects, the objectives and the procedure of the study were explained in detail to them & their informed written consent were taken. A standard questionnaire was filled after taking history and through clinical examinations. All study procedures were maintained at the Model Family Planning Clinic, Rangpur Medical College & Hospital. At first five (5) ml of blood was collected from antecubital vein from each subject under all aseptic precaution by a disposable syringe. The needle was detached from the nozzle and then blood was immediately transferred into a test tube which containing EDTA (ethylene diamine tetra acetate) an anticoagulant. Then the test tube was rolled gently between two pump for proper mixing of anticoagulant with blood and immediately taken to the laboratory. Then RBC & PCV were studied with an automatic electronic blood count analyzer at the department of biochemistry, Rangpur medical college, Rangpur.

Result:

Mean \pm SD value of RBC and PCV were (4.7618 \pm 0.36697, 40.978 \pm 1.9973) in group A and (4.6569 \pm 0.48947,

36.944 \pm 2.4116) in group B. The data depicted in table -I and table II shows difference of RBC and PCV in rural than those of healthy control urban women.

Table I: Showing mean \pm SD total count of red blood cell in group A and group B

Group	Total count of red blood cell Mean \pm SD million/ μ L	't' value	'p' value
A n= 50	4.7618 \pm 0.36697	1.280	>0.05 ^{ns}
B n = 50	4.6569 \pm 0.48947		

Table II: Showing mean \pm SD packed cell volume in group A and group B

Group	Packed cell volume(PCV) Mean \pm SD %	't' value	'p' value
A n= 50	40.978 \pm 1.9973	9.687	<0.001 ^{***}
B n = 50	36.944 \pm 2.4116		

A = Urban women of reproductive age (Control), B = Rural women of reproductive age (Experimental), n = Number of subjects, SD = Standard deviation, ns=non significant, *** =p<0.001^{***}. Data were expressed as Mean \pm SD, figures in parenthesis indicates ranges.

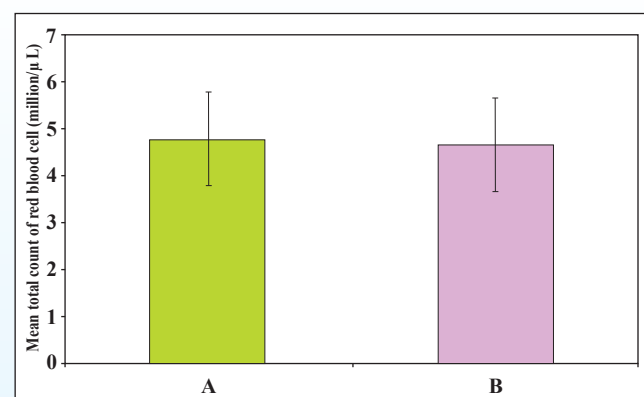


Figure 1: Diagram showing mean of total count of red blood cell in group A and group B

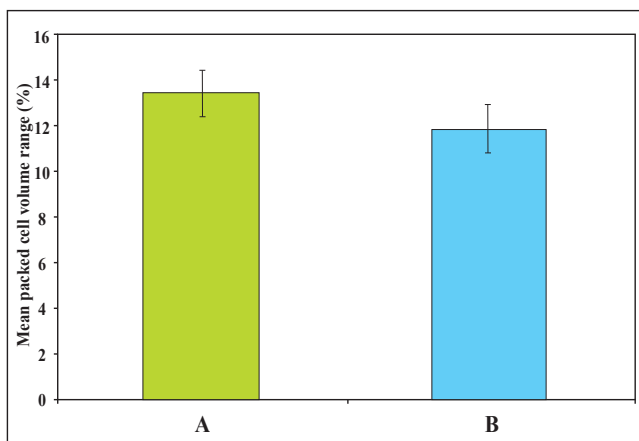


Figure 2: Diagram showing mean packed cell volume in group A and group B

Discussion:

In this study, the mean total count of red blood cell and packed cell volume were decreased in rural women of reproductive age than those of control subjects. This finding is in agreement with those reported by Sengupta & Chakrabarti,⁶ Chakraboti,⁸ Modjadj, Albert & Mamabolo,¹⁰ Al-Sayes et al¹¹. They observed that total count of red blood cell and packed cell volume were decreases in rural women of reproductive age which might be due low dietary intake such as low consumption of red meat, vegetables, cereals and fruits. So, lack of these factors causes deficiency of protein, iron, vitamin B₁₂, vit C, vit A, folate and others minerals. Iron is essential for the synthesis of heam portion of hemoglobin, the iron containing enzymes essential for electron transfer and oxidation reduction reaction. Protein of high biological value in the diet is essential to supply amino acid for the synthesis of globin portion of hemoglobin. Folates are vital for cell division and homeostasis because of the essential role of folate-containing co-enzymes in nucleic acid synthesis, methionine regeneration and the shuttling, oxidation and reduction of one carbon units required for normal metabolism and regulation. Ascorbic acid is act as reducing agent. It reduces ferric iron to ferrous form in the stomach and thus helps iron absorption. It may also play a role in folate metabolism. Chronic blood loss due to infection such as malaria and hookworm infestations plays a vital role. The hookworm provokes damage to the villi, resulting in blood loss and anti-coagulant production, which promote continuous bleeding. Micronutrient deficiency has been considered a prime factor for decrease total count of red blood cell and PCV. Most of the rural women are disadvantaged people in the world in terms of their health

status and access to accurate and appropriate health information, adequate and affordable health services. Sexual and reproductive health is a particular concern for rural women, as a host of social, cultural, political, and economic factors increase rural women's vulnerabilities to pregnancy and childbirth related deaths, disabilities and unsafe abortion. All of these factors causes decrease total count of red blood cells and PCV in rural women of reproductive age.

Conclusion:

In the present study, it was difficult to comment the exact causes involved for these changes in rural women of reproductive age. It may be included that red blood cell & PCV status is most likely related to some nutritional deficiency. Such as protein, iron, vitB₆, vit C. All of these factors cause decreased total count of red blood cell & PCV in rural women of reproductive age. These factors are essential for increased hematological status. In order to improve women's hematological status, policy should focus on creating opportunities to increase agricultural productivity, promote health service and emphasize women health education in the rural women of reproductive age.

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Notch Signaling Pathway in Cancer Stem Cells: A Review

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Abstract:

Over the years, cancer stem cells have been increasingly identified in many malignancies. Although, the origin and mechanism remains controversial, which typically demonstrate persistent activation of one or more highly conserved signal transduction pathways involved in embryogenesis, development and tissue homeostasis. However, dysfunctions of these pathways are evident in multiple tumor types. Specifically, aberrant activation of these pathways plays a crucial role in the modulation of cancer stem cells, which generally have slow growth rates and resistant to chemotherapy or radiotherapy. Thus, new treatment strategies targeting these pathways to control stem cell replication, survival and differentiation are under development. In this review, we will discuss the role of the Notch pathway in cancer stem cells and implication of Notch inhibitors in cancer treatment outcomes.

Key words: NECD-notch extracellular domain; NICD-notch intracellular domain; TM-transmembrane domain; endoplasmic reticulum; γ secretase inhibitors; DAPT; IL-X.

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Introduction:

CSCs is a general term referring to the cancer cells capable of differentiation and self-renewal of diseases, which plays a crucial role in chemotherapy resistance¹. In general, some cells in a tumor may undergo some sort of genetic or epigenetic changes followed by dysfunction of cell signaling cascades included Notch pathway,² which plays an important role in cell proliferation, differentiation, development and homeostasis³. Although, this deregulated Notch signaling is found in various diseases, such as T-cell leukemia, breast cancer, prostate cancer, colorectal cancer, lung cancer as well as central nervous system (CNS) malignancies⁴. Recent evidence has demonstrated that Notch signaling is associated with head and neck cancer

stem cells⁵. Therefore, pharmacological inhibitions of this pathway can overcome self-renewal of diseases and chemoresistance.

Concept of Notch signaling pathway: Notch signaling is an evolutionary conserved pathway in multicellular organisms, which regulates cell-fate determination and maintains tissue homeostasis. Receptors for Notch signaling are single-pass transmembrane proteins composed of functional extracellular NECD, TM and NICD, where receptors are processed in the ER and Golgi within the signal-receiving cell through cleavage and glycosylation, generating a Ca²⁺-stabilized heterodimer composed of NECD noncovalently attached to the TM-NICD inserted in the membrane (S1 cleavage).

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In mammalian signal-sending cells, members of the Delta-like (DLL1, DLL3, DLL4) and the Jagged (JAG1, JAG2) families serve as ligands for Notch signaling receptors. Upon ligand binding, the NECD is cleaved away (S2 cleavage) from the TM-NICD domain by TAØE (TNF-ADAM metalloprotease converting enzyme). The NECD remains bound to the ligand and this complex undergoes endocytosis/ recycling within the signal-sending cell in a manner dependent on ubiquitination by Mib. In the signal-receiving cell, -secretase (also involved in Alzheimer's disease) releases the NICD from the TM (S3 cleavage), which allows for nuclear translocation where it associates with the CSL transcription factor complex, resulting in the subsequent activation of the Notch target genes: Myc, p21, and the HES-family members⁶⁻¹⁴. Therefore, the Notch signaling pathway has spurred interest for pharmacological intervention due to its connection with

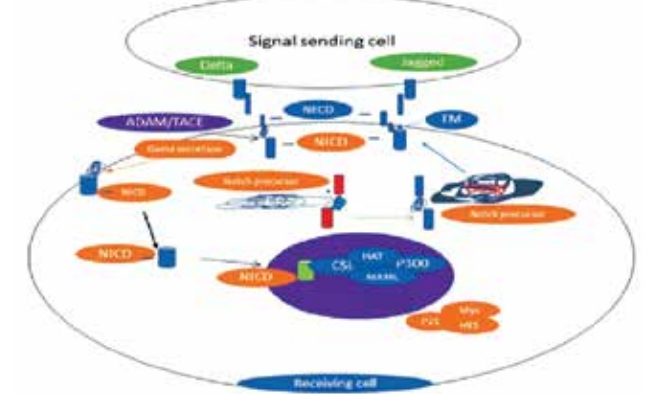


Figure 1: An overview of Notch signaling pathway and proteolytic processing.

Origin and identification cancer stem cells: Mainly two hypotheses exist regarding the origin of CSCs:³

1. Originating from a somatic tissue cell that undergoes genetic mutations, becomes cancerous, and acquires stem characteristics.
2. Derivation from embryonic stem or adult cells as a result of genetic mutations. The mode of onset may depend on the location of the origin of the tumor.

However, currently, three hypotheses are discussed:⁵

1. Source of "normal" stem cells with cancerous phenotype
2. Source of differentiated cells with oncogenic mutation (Return to self-regeneration and multipotency)

3. Fusion of stem cells with tumor cells (much discussed with the formation of bone metastases)

In contrast, identification and isolation of cancer stem cells constitute a major experimental challenge. Researchers attempt to isolate these cells by identifying properties that distinguish stem cells from their differentiated progeny and from stromal cells. The methods used for the identification and isolation of tumor stem cell populations apply the same techniques used to identify normal stem cells from their differentiated progeny. Cancer stem cells can be identified via surface markers

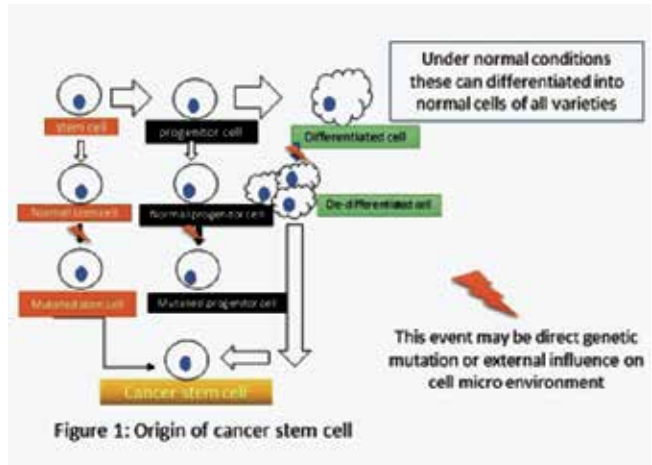


Table I: Cancer stem cell marker reported in individual studies

Study type	Cell surface markers	References
Myeloid leukemia	(AML)CD34+, CD38 ⁺	15-16
Breast cancer	EPCAM(ESA)+, CD44+,CD24 ⁻	17-18
Ovarian cancer	ALDH, CD29, CD133	19
Glioblastoma	CD133+, CD15+	20
Medulloblastoma	CD133+, CD15+	21
NSCLC	CD133+	22
Hepatocellular carcinoma	CD45, CD90+	23
Colon cancer	CD133+,CD44+,CD26+,ALDH	24
Prostate cancer	CD44+, CD133+, CD49	17
Melanoma	CD20+, CD271+	25
Pancreatic adenocarcinoma	CD44+, CD24+	23
HNSCC	CD44+,CD133, ALDH1	26
Lung cancer	CD133+,CD90,CD117,ALDH1	27

HNSCC= head and neck squamous cell carcinoma; NSCLC= nonsmall cell lung carcinoma

Role of Notch inhibitors in cancer stem cells: Because the Notch signaling plays an important role in cancer development, it is plausible that targeting the Notch signaling steps can have antitumor effects^{15,16}. Currently, one of the emerging approaches for blocking Notch signaling is to suppress the proteolytic step that leads to the

On ligand binding, Notch receptors undergo a series of programs proteolytic events, first by γ -secretase at the extracellular surface, which leads to liberation of the extracellular fragment, and then by intramembranous cleavage mediated by γ -secretase. NICD is then released from the inner surface of cell membrane and is translocated into the nucleus where it activates transcription of the target genes (Fig 1).¹⁷

Over the past decades, inhibitors for γ -secretase have been actively investigated for their potential to block the Notch receptor activation, several forms of γ -secretase inhibitors have been tested for antitumor effects. First, an original γ -secretase inhibitor, IL-X was shown to have Notch1-dependent anti neoplastic activity in Ras-transformed fibroblasts. More recently, tripeptide γ -secretase inhibitor was reported to suppress tumor growth in cell lines and/or xenografts in mice from melanoma and Kaposi sarcoma¹⁸. Treatment with dipeptide γ -secretase inhibitor N-[N-(3, 5-difluorophenacetyl)- L-alanyl]- S-phenylglycine t-butyl ester (DAPT) also resulted in a marked reduction in medulloblastoma growth and induced G 0 -G 1 cell cycle arrest and apoptosis in a T-ALL animal model^{19,20}.

Another γ -secretase inhibitor, dibenzazepine, has been shown to inhibit epithelial cell proliferation and induce goblet cell differentiation²¹. Furthermore, a phase I clinical trial for a Notch inhibitor, MK0752 (developed by Merck, Whitehouse Station, NJ) has been launched for relapsed or refractory T-ALL patients and advanced breast cancers. Besides the evidence of γ -secretase inhibitors in directly inactivating Notch signaling in cancer cells, γ -secretase inhibitors may also suppress angiogenesis in solid tumors by interfering in the crosstalk between the tumor and vasculature through the Notch signaling²². The exciting studies summarized above strongly suggest a potential clinical application of γ -secretase inhibitors in cancer therapeutics. However, one of the major challenges on the way toward this goal is the untoward side effects associated with the inhibitors, especially the cytotoxicity in the gastrointestinal tract,²³ which can be exacerbated by conventional chemotherapeutic drugs. Therefore, balancing efficacy and toxicity γ -secretase inhibitors must be considered in future clinical applications.

Table II: Clinical trials employing γ -secretase inhibitors in cancer

Name	Tumor	Study type	Enrollment	Primary endpoint	Trial ID	Ref.
MK-0752	AST	Phase I	103	MTD	00106145	37
RO-4929097			17	PKS	01218620	NR
RO-4929097			28	Safety	01096355	NR
RO-4929097+capcitabine			30	MTD	01158274	41
RO-4929097+gemcitabine			18	Safety	01145456	42
RO-4929097+temsirolimus			17	Safety	01198184	43
MK-0752+gemcitabine	PC	Phase I	44	Safety	01098344	NR
		Phase II		MTD		
RO-4929097		Phase II	18	Survival rate	01232829	44
MK-0752+docetaxel	BC	Phase I/II	30	DLT	00645333	38
RO-4929097	RCC	Phase I/II	5	Efficacy	01141569	NR
RO-4929097	CC	Phase II	37	Efficacy	01166867	40
RO-4929097	NSCLC	Phase II	6	Efficacy	01193863	NR

NR= Not reported; MTD= Maximum tolerating dose; DLT= Dose relating toxicity; NSCLC= Non-small cell lung cancer; PKS= Pharmacokinetics study; AST= Advanced solid tumor; PC= Prostate cancer; BC= Breast cancer; RCC= Renal cell carcinoma; CC= Colorectal carcinoma

Future implications: For controlling both developmental processes and tumorigenesis, Notch signaling pathway is very important. However, deregulation of this pathway frequently observed in many cancers through mutations and amplification of the components. In contrast, recent studies suggest that one of the most promising targets in inactivating the Notch signaling is γ -secretase complex, because accumulating preclinical studies have shown that γ -secretase inhibitors hold promise as a new target-based therapy for those tumors with Notch activation. However, before Notch based therapy becomes a reality, future studies should primarily focus on the issues of target specificity and address the possible side effects that may affect cancer patients who receive this new treatment regimen and additionally, Notch inhibitors combined with chemotherapy or radiotherapy hold great promise for cancer treatment modulation.

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Ceramage Inlay: A Case Report

Shanta KN¹, Bashar AKM², Shikder AHM ZH³

Abstract:

One of the primary challenges faced by today's dental restorative team is the need to deliver high-strength restorative options without compromising the esthetic outcome fueled by ever-increasing patient demands. The availability of improved ceramic materials, bonding techniques, new technology and issues of amalgam safety have led to a revival of interest in ceramic inlays in dentistry over the past ten years. The increased demand for esthetically pleasing restorations has led to the introduction of new all ceramic materials together with improvements in resin bonding agents. Bonded ceramic inlays can eliminate the need for conventional means of retention and allow the restoration of lost tooth structure. Ceramage, the micro ceramics have excellent biocompatibility, inertness, improved physical bonding, and natural appearance. In this case report, a patient came with mesial caries on upper left 1st molar. After diagnosing class-II carious lesion Ceramage inlay was prepared and follow up revealed significant pleasant outcome.

Key words: Ceramage, Inlay, Composit.

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Introduction:

Increased interest in tooth-colored non-metallic posterior restorations has stimulated the development of new materials. The first attempt to use esthetic inlays were described during the end of the nineteenth century¹. Several systems and techniques are available today for tooth-colored inlays using both resin composite, all-ceramic materials, ceramage but few studies have evaluated these materials longitudinally². Such a new material is Ceramage, which combines the advantages of ceramics and composite both. Ceramage is a micro ceramic polymer system with 73% of zirconium silicate filler (PFS-Progressive Fine Structured filler) supported by an organic polymer matrix which exhibits superior flexural strength, elastic properties, ensures a durable surface quality with excellent polishability and high resistance to plaque. This extraordinary structure of ceramage shows properties similar to porcelain making it an ideal choice for posterior restorations. Additional to the physical properties a light transmission very close to that of natural dentine and enamel had been integrated into Ceramage. Ceramage is an easy-to-apply paste, accurate reproduction of the natural tooth shade, its abrasion resistance ensures molars are

protected from the opposing dentition, flowable Composite Resin suitable for adjustments to the build-up and repairing small areas, in combination with M.L. Primer produces a strong bond to any type of metal, including precious alloys (brushier). Due to its strength and versatility, the material can be used for a wide range of clinical applications, including highly aesthetic anterior and molar restorations that require long-term durability, for example: anterior/posterior crowns, inlays/onlays, veneers, thin veneers, telescopic crowns, implant restorations, anterior three-unit bridgework (press only), Indirect and direct repairs of crown restorations and defects in prosthetic restorations³. In this report, inlay is prepared with Ceramage on class-II carious lesion.

Case Report:

An 18 year old female patient reported to the Department of Conservative Dentistry and Endodontics with the chief complaint of food lodgement in left upper back teeth region since 2 months. The medical history of the patient was non-contributory. On clinical examination, a class-II carious lesion was present on the mesial aspect.

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The tooth was asymptomatic and no pain could be elicited. The tooth responded positively to the thermal and electric pulp testing. The involved tooth showed no signs of mobility. Her radiographic examination revealed the presence of a carious lesion approaching but not involving the pulp with no signs of apical involvement. The patient's informed consent and necessary ethical clearance were obtained.

Clinical Procedure

Isolation of the tooth was done with cotton roll and saliva ejector. Inlay cavity was prepared using 45 no. flat ended fissure bur with maintaining standard protocol. The occlusal walls were vertical or slightly divergent. The impression was taken and temporary restoration was placed into the inlay cavity. After preparation of model, a thin layer of ceramage spacer applied on prepared cavity with supplied brush, followed by application of ceramage separator, then ceramage flow applied and cured for 30 seconds in solidilite light box. Then application of ceramage dentin and cured for 3 minutes and build up of enamel by ceramage composite. After build up of enamel oxy barrier was applied and final curing was done for 3 minutes by tungsten halogen light. After curing, contouring of the restoration was done with the help of robot carbide fissure bur. Finally, finishing and polishing of the restoration was done by ceramage finishing and polishing kit. Temporary restoration was removed from cavity on the next day. Cavity was cleaned and dried. Before insertion, the internal inlay surface and the cavity walls were coated with a dual polymerizing resin composite, and then the inlay was placed into the cavity. The surplus material was removed using a dental probe. Resin composite was polymerized for 60 seconds by tungsten halogen light. Finishing of the definitively set inlay was carried out using super snap polishing kit. Occlusion and articulation assessment was carried out using articulating paper.



Fig: Materials & Instruments : Ceramage Spacer, Ceramage Separator, Ceramage body, Ceramage Enamel, Ceramage modeling liquid, Ceramage Oxy barrier, Solidilite light box, Ceramage polishing kit, Polishing paste (Dura polish), Polishing paste (Dura polish Dia)



Fig: Clinical steps of ceramage inlay, Ceramage tube

The patient was observed clinically after 7 days and two year for restoration for pain, sensitivity, marginal adaptation, crack formation, fracture and discoloration. There was no pain, no sensitivity, no marginal deterioration, no crack formation, no fracture and no discoloration even after two years of restoration. Radiographs after 7 days of restoration also shows there is no development marginal gap and secondary caries around the restoration.

Discussion:

As the aesthetic aspect of dental care becomes important to patients, aesthetics is playing an increasingly important role in their choice for dental restorations. There are various options of aesthetic restoration for posterior teeth include direct composite restoration, indirect composite restoration, metal ceramic restoration, all ceramic restoration. Direct composite is generally used for small to medium size preparation and can be placed in one appointment but there are certain reasons like difficulty in placement, improper marginal adaptation, difficulty in finishing & in developing contour and contacts, chances of voids which leads to weakening of the restoration, chances for microleakage and post-operative sensitivity. So it becomes difficult to use in day to day practice. Indirect composite restorations provide good color match, easy to finish, intra oral repair is possible but there are chances of poor marginal fit, marginal failure, require laboratory support, technique sensitive, adhesion to tooth may be weak. Metal ceramic restorations for small to medium size carious lesion in posterior teeth are difficult to fabricate and do not provide good aesthetics. Metal ceramic is generally used for full coverage restoration. All ceramic material as well as with ceramage, with high strength provide good restorative alternative to moderate to large size carious lesion. Cavity preparation is also simple. All

ceramic restoration is very near to ceramage. In one study clinical assessment and survival rate ceramic inlay showed that the lack of recurrent caries, the only slight changes in marginal discoloration and colour match, combined with the excellent longevity prove that ceramic inlays are a valuable tool for the restoration of posterior teeth⁴.

Evaluation of clinical performance of ceramic inlay and composite inlay proved that posterior tooth-colour inlays exhibited a success rate of 100% for ceramic inlays and 90% for composite inlays even if placed by relatively inexperienced but supervised student operators⁵. Evaluation the performance of Class II Cerec inlays after 10 years of clinical service found that patient satisfaction with and acceptance of the ceramic inlays were high, and the performance after 10 years of clinical service was acceptable⁶. Clinical study by R. T. Lange showed that indirectly manufactured Evopress ceramic inlays performed better than direct Filtek Z250 composite restorations in marginal adaptation, colour match and anatomic form⁷.

Conclusion:

Ceramage inlay is a better alternative as esthetic restoration compared to direct and indirect composite resin restoration for medium to large size carious lesion. More studies are required to know long term performance of ceramage inlay.

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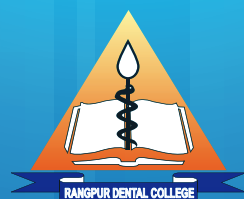
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