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Association Between Gingival Enlargement and Anti-hypertensive Drugs- A retrospective study

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ABSTRACT:

Hypertension is also termed as high blood pressure. It can lead to severe health issues thereby increasing the risk of cardiovascular disease, stroke, culminating in death. The force that an individual's blood is exerted against the ventricular and arterial walls of blood vessels is termed as blood pressure. This pressure is elicited based on the resistance of the blood vessels and how much of the cardiac output is. There are various methods to cope with hypertension such as diet modification, exercise, meditation and medication The aim of the study is to determine the association between gingival enlargement and anti hypertensive drugs.. A very common adverse effect of these drugs is gingival enlargement in the oral cavity. The enlargement of the gums caused due to anti-hypertensive drugs commences, due to their reactions in patients treated with anticonvulsants, immunosuppressants and calcium channel blockers. The data collected from the records were 86000 and they were screened for patients with drug induced gingival enlargement. The collected data was tabulated in excel sheet and imported to spss software for statistical analysis. From the study, 45 patients were diagnosed with drug induced gingival enlargement out of which, 24 patients were males and 21 patients were females. Predominant gender is male. Among the age groups, group 1[20-30 years] had 6 patients, group 2[36-50 years] had 16 patients and group 3[51-70 years] had 23 patients. The predominant age group was group 3[51-70 years]. Among the type of drug used, gingival enlargement, amlodipine induced gingival enlargement was seen in 78%, nifedipine induced gingival enlargement was seen in 13%. Therefore, to conclude, the predominant drug induced gingival enlargement, was amlodipine in this study and the predominant age group was group 3 [51-70 years].

Keywords:

Amlodipine, Cardiovascular, Drug, Enlargement, Gingiva, Hypertensive.

INTRODUCTION:

The condition wherein there's overgrowth or hyperplasia of the gingiva that is elicited due to the administration of drugs which is used to treat hypertension,are called drug induced gingival enlargement. Hypertension is a major condition affecting billions of people globally. It elicits emotional changes, systemic ailments which not only affects systemically but also affects oral cavity. Moreover, leads to cardiovascular events, cardiac death and kidney disease (1). Hypertension related complications pose a major risk and their development is continuous, starting at a blood pressure level as low as 115/75 mmHg.The major aspect behind diagnosing hypertension is accurate measurements of blood pressure. Improper positioning of the hand, inadequate BP cuff size, and insufficient relaxing time[<5 minutes] prior to BP measurements are some of the usual errors which elicit falsely elevated readings (2).

Various numbers of medication classes lie, to facilitate healthcare workers and providers in treating their patients with hypertension. These include β-blockers, diuretics, ACE inhibitors, angiotensin receptor blockers and calcium channel blockers. Some of the most common and oldest of antihypertensives, the calcium channel blockers are a heterogeneous group of medications. Most employed anti-hypertensive drugs given to a patient to treat hypertension are amlodipine, nifedipine and verapamil (3) . Amlodipine is a long-acting, lipophilic, third generation dihydropyridine and a slow calcium ion or channel blocker. It's mechanism of action is the influx of calcium ions into vascular smooth muscle and cardiac muscle thereby decreasing peripheral vascular resistance. Nifedipine is also a dihydropyridine calcium channel blocker. It's short acting formulation is attributed with reflex sympathetic nervous system activation culminating in flushing, tachycardia, worsening myocardial ischemia, and cerebrovascular ischemia. Extended release formulations are also available and are as effective as ARBs, β-blockers, and diuretics. Verapamil is an anticonvulsant and antiepileptic drug. It may also be used for certain heart arrhythmias or neuropathic pain. It can be taken intravenously or orally (4), (5). Studies show that the activity and responsiveness of fibroblasts to these drugs is eliminated under non-inflammatory conditions. The chronic use of such drugs causes gingival enlargement wherein plaque control measures must be implemented as a first line of treatment along with drug replacement in order to prevent periodontal destruction (6),(7) . In such cases of periodontal destruction, periodontal therapy is done to treat the existing and prevent further breakdown (8,9). Several regenerative methods are also employed in the repair of periodontal breakdown by the use of guided tissue regenerative methods and by the use of stem cells (10,11). The esthetic restoration is done by gingivectomy and gingivoplasty using lasers and lip repositioning(12).

It is estimated that around 85% of the adults who are chronic users of anti-hypertensive drugs, had gingival overgrowth. It's severity is seen in the 6th month of consumption. Dosage reduction or replacement of anti-hypertensive drugs was the first line of treatment for drug induced gingival enlargement. Metoprolol [50mg] is a good replacement (12,13). There has been no clear demonstration which could consolidate the pathogenesis, clinical symptoms and signs, and the management of affected patients. But when it comes to drugs related to cardiovascular drugs, there is a necessity of exposure to knowledge about known drugs and familiarize with newest drugs to date. Previously our team has a rich experience in working on various research projects across multiple disciplines(14–16)(17–28).The above clinical trials and systematic reviews performed in the previous studies led to the idea for the current retrospective epidemiological study which aims to associate the relationship between drug induced gingival enlargement and anti hypertensive drugs as well as to determine the predominant drug causing hypertension.

MATERIALS AND METHODS:

Sampling:

Non-probability sampling was collected from June 2019 to March 2020. The case sheets of the patients above 18 years of age who had reported to Saveetha Dental college for the treatment of gingival enlargement were reviewed. The external validity was good, as it is generalisable among patients of the same ethnic origins within the state and country.

Ethical approval

Ethical approval was obtained from the Institutional Ethical Committee and scientific review board [SRB] of Saveetha Dental College. SDC/SIHEC/2020/DIAS/DATA/0619-0320

Data Collection:

The data collected from june 2019 to march 2020 after screening 86000 records and study subjects were selected based on the parameters such as patient's name, age, gender, diagnosis and the type of treatment done. Among the 86000 records, patients with anti-hypertensive drug induced gingival enlargement were considered for the study. The type of drugs included are amlodipine, nifedipine and verapamil. To estimate the predominant age group, patients were divided into 3 age groups and generalised and localised types of gingival enlargement were recorded seperately. The sample size of the study was 45 patients. The data was collected and tabulated in the excel sheet and imported to spss software for statistical analysis.

Statistical analysis:

The data was imported to spss software by IBM version 25.0 for Windows OS in which the output variables were defined. The independent variables were age and gender whereas the dependent variables were the type of drug used and the statistical mean value obtained. The statistical test used was correlation test to establish the results.

Methodology:

The study patients diagnosed with drug induced gingival enlargement were collected from DIAS records and divided into three groups based on their age.
Group 1: 25-30 years
Group 2: 36-50 years
Group 3: 51-70 years
The most predominant age group and gender with anti-hypertensive drug induced gingival enlargement were estimated and correlated using chi-square analysis.

RESULTS:

From this study, it was estimated that among 45 patients were diagnosed with drug induced gingival enlargement, 24 patients were males and 21 patients were females. From figure 1, it can be estimated that the predominant gender is male.Among the type of drug used, gingival enlargement, amlodipine induced gingival enlargement was seen in 78%, nifedipine induced gingival enlargement was seen in 13%. Figure elicited the aspect that the predominant drug induced gingival enlargement was amlodipine in this study. Among the age groups, group 1[20-30 years] had 6 patients, group 2[36-50 years] had 16 patients and group 3[51-70 years] had 23 patients. From figure III, the predominant age group was group 3[51-70 years] with 23 patients. Based on figure IV, it can be inferred that the majority of cases both localized and generalised enlargement was higher among the age group 51-70 years. Chi square test was done and p value obtained was 0.958 which was not statistically significant. Based on figure 5 it can be inferred that the majority of cases had amlodipine induced gingival enlargement. Chi square test was done and p value was 0.053 which was statistically significant. Figure 6 demonstrated that the majority of cases with drug induced gingival enlargement were males with predominantly generalised type of enlargement. Chi square test was done and p value obtained was 0.096 was not statistically significant. Figure 7 showed it can be inferred that the majority of cases with drug induced gingival enlargement were males with predominantly amlodipine induced enlargement. Chi square test was done and p value obtained was 0.421 was not statistically significant.

DISCUSSION:

Fay AA et al, 2005 and Ikawa K et al, 2002, discussed the 3 major drugs that cause gingival enlargement based on their dosage and the patient. They are amlodipine, nifedipine and verapamil wherein all the 3 drugs elicit a similar mechanism of action. They act at a cellular level inhibiting intracellular calcium ion influx despite their pharmacological diversity (29,30). Lafzi A et al, 2006, discussed the necessity to comprehend the mechanism of action to determine the common adverse effect of all 3 drugs on the secondary target tissue such as gingival connective tissue. Madi M et al, 2010 discussed the gingival enlargement leading to gingival pocket formation, food accumulation, culminating in serious periodontal issues. Long term prognosis can lead to periodontitis, thereby causing mobility of the teeth adhering to the affected gums. This poses an esthetic concern as well as partial or complete loss of dentition (31,32).

Mavrogiannis M et al, 2006, demonstrated that there is an excessive plaque formation leading to secondary inflammation. The gingival overgrowth or inflammation is elicited by fibroblasts, inflammatory cytokines, matrix metalloproteinases(33). A study by Dhalle RP et al, 2009, said that they also have control over synthesis and functions of collagenases (2,33). A study by Pradhan et al proved 81.2% of patients in his study had gingival enlargement due to amlodipine (34). Jayanthi R et al demonstrated that 76% of patients had amlodipine induced gingival enlargement (35). Substitution with metoprolol and its success rate was also demonstrated in a study by Biswas et al 2019 (36). In our study, graph 1 indicated distribution of study population based on gender, graph 2 indicated type of gingival enlargement, graph 3 indicated on type of drug and graph 4 indicated the age group.

A study by Seymour RA et al showed amlodipine had 70% involvement in gingival overgrowth and study by Lederman D et al showed 36% of the patients were nifedipine induced and the rest were amlodipine induced (37),(38). Similar results were demonstrated by Jorgensen MG et al in their systematic review(39). Kantarci et al discussed that there were significantly higher numbers of basal membrane discontinuities in the tissues. These findings provide a hypothesis that gingival enlargement culminates in compromised basal membrane structure and increased interactions between epithelial and connective tissue membrane that cause fibrosis (39,40) A study by Subramani et al formulated a hypothesis demonstrating mast cells eliciting many inflammatory diseases associated with fibrosis (41). The cyclosporine can modulate the renin-angiotensin system and its receptors in the gingival tissue. Kaur G et al, 2010 discussed the alterations caused in the renin angiotensin mechanism and its effect on the gingival fibroblast cells, causing gingival overgrowth. Clinical manifestations of gingival enlargement appears within 1-3 months after initiation of treatment with these medications (42).Limitations: The data may have discrepancies and it is limited to patients with gingival enlargement confined to one particular geographic location. The study does not include drugs other than anti-epileptics, antihypertensives and calcium channel blockers Future scope: The study gives a vast idea on gingival enlargement, drugs causing gingival enlargement, type of spread of disease,mode of prevention and treatment modalities. Our institution is passionate about high quality evidence based research and has excelled in various fields ((43–53).

CONCLUSION:

From this study it can be concluded that the predominant drug that causes gingival enlargement was amlodipine, the predominant gender involved was male and the most predominant age group prone to gingival enlargement was 51-70 years. Awareness on common drug usage, its contraindications and adverse effects is necessary to prevent such complications arising from the usage of random drugs such that use of over the counter drugs can be prevented. Patients are also instructed on proper medical visits to treat systemic disorders by medical professionals in order to avoid drug induced complications and counteract such adverse effects.

Author Contributions:

First author [Nivesh Krishna R] performed analysis,interpretation and wrote the manuscript. Second author [Dr.Sankari] contributed to conception,data designs,analysis,interpretation and critically revised the manuscript. Third author [Dr.Arvind S] participated in the study and revised the manuscript. All the three authors have discussed the results and contributed to the final manuscript.

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Conflict Of Interest: Nil.

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FIGURES:

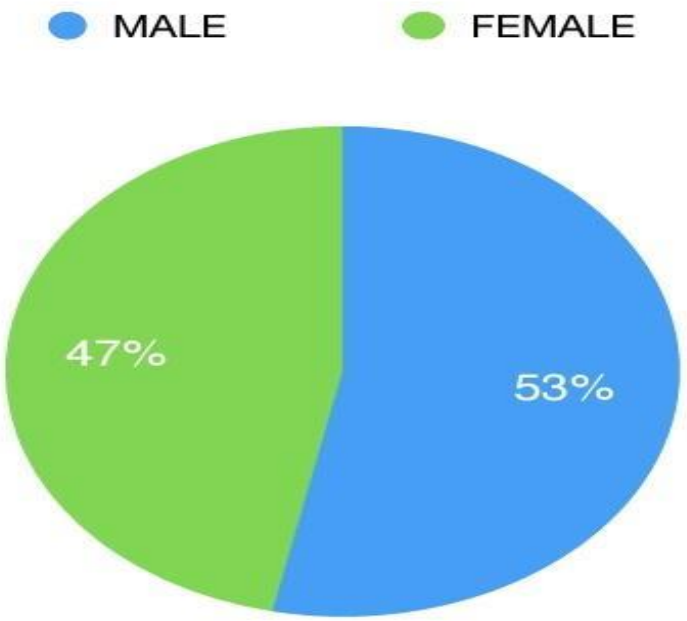

Figure 1 denotes the distribution of study population based on gender. Sample size was 45 patients. Among the study population, 24 patients were males and 21 patients were females. In the below graph, blue colour denotes the percentage of male patients [53%] and green colour denotes the percentage of female patients [47%]. The predominant gender was male.

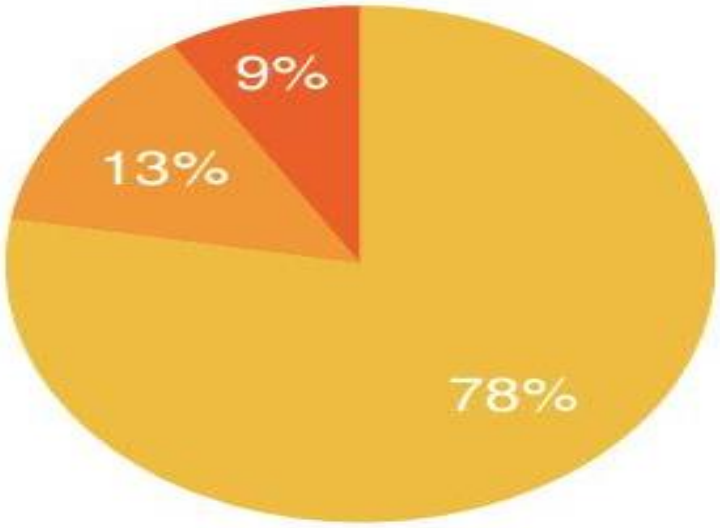

Figure 2 denotes the distribution of study population based on the type of drug used. Sample size was 45 patients. It can be estimated that among 45 patients who were diagnosed with drug induced gingival enlargement, 35 patients[78%] had amlodipine, 6 patients[13%] had nifedipine and 4 patients[9%] had verapamil induced gingival enlargement. In the figure, the colour yellow denotes amlodipine, orange denotes nifedipine and red colour denotes verapamil. It can be inferred that gingival enlargement was commonly seen among amlodipine users when compared to nifedipine and verapamil.

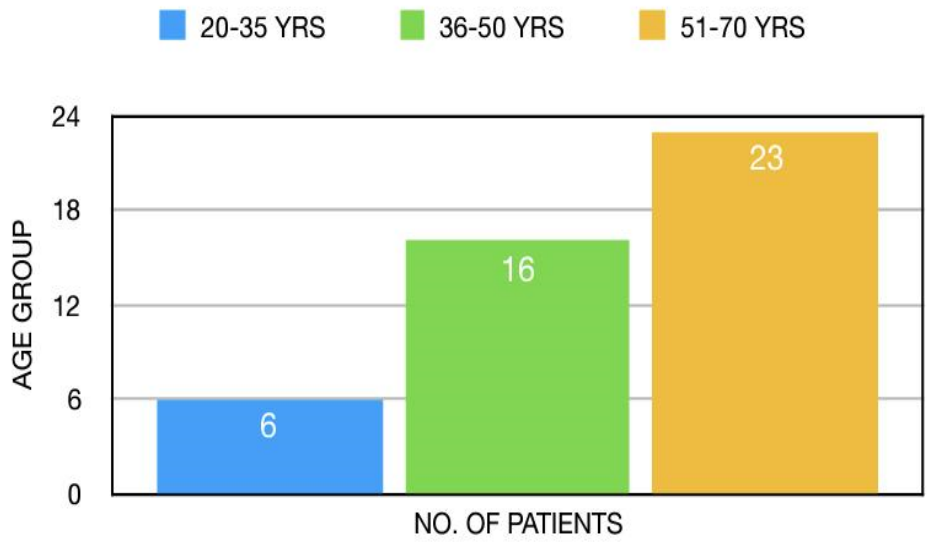

Figure 3 denotes the distribution of study population based on age group. Sample size was 45 patients. X axis indicates the number of patients among 45 patients and Y axis indicates the age group of 45 cases. The patients are divided into 3 age groups, 18-35 years [group-1], 36-50 years [group-2]and 51-70 years [group-3]respectively. In the figure, group-1[blue]6 patients , group-2 [green]16 patients and group-3 [yellow] 23 patients.Gingival enlargement was predominantly seen among group-3 patients[51-70 years] with 23 patients among 45 patients.

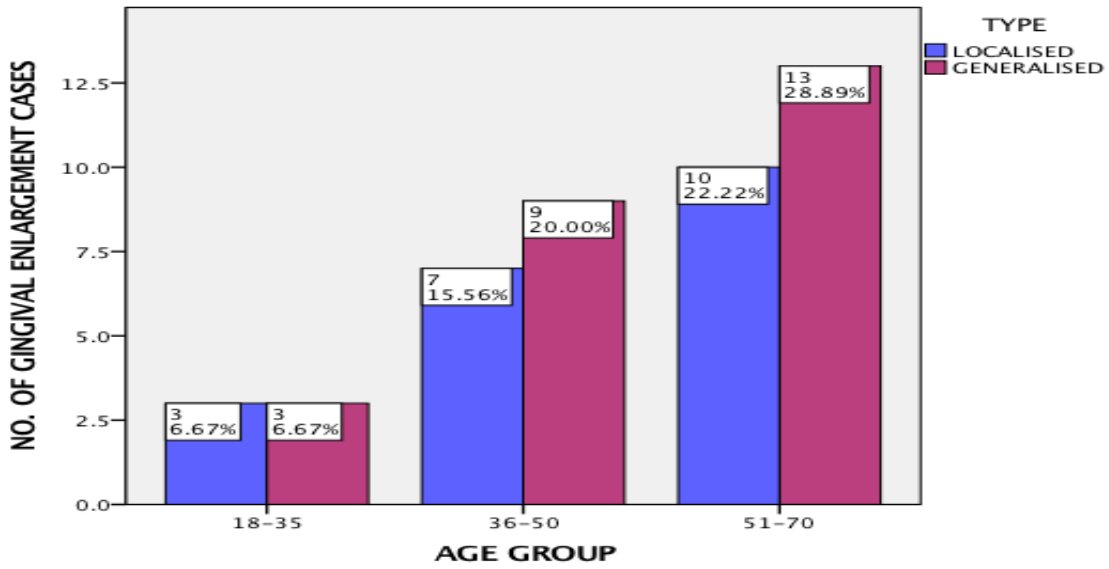

Figure 4 denotes the association between age group and type of disease. X axis indicates the age group of the 45 patients and Y axis indicates the number of cases with generalised or localised gingival enlargement among 45 cases .In the figure, colour blue denotes the localised variant [20 patients] and colour pink denotes the generalised variant[25 patients]. Chi square test was done and p value obtained was 0.958, thus was not statistically significant. Based on

this fig 4 it can be inferred that the majority of cases both localized and generalised enlargement was higher among the age group 51-70 years but however association was not statistically significant.

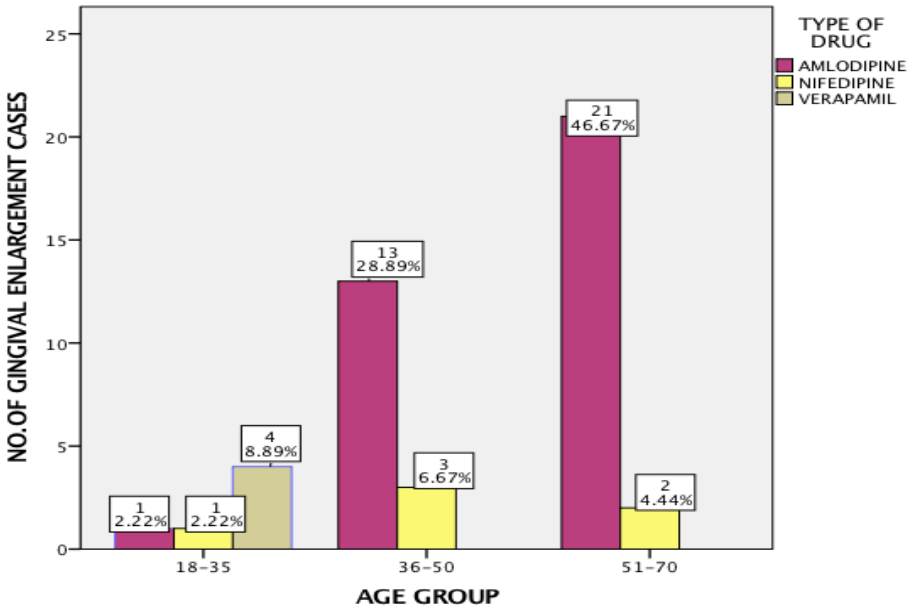

Figure 5 denotes the Association between age group and type of drug used amlodipine, nifedipine and verapamil. X axis indicates the age group of 45 patients and Y axis indicates the number of cases using the three types of drugs among 45 patients. It can be estimated that among 45 patients who were diagnosed with drug induced gingival enlargement, 35 patients had amlodipine, 6 patients had nifedipine and 4 patients had verapamil induced gingival enlargement. In the figure, colour pink [amlodipine,] yellow [nifedipine]and light brown [verapamil]. The association between age groups and types of drugs. Chi square test was done and p value was 0.053 which was statistically significant. Based on this figure 5, it can be inferred that the majority of cases had amlodipine induced gingival enlargement and association was statistically significant.

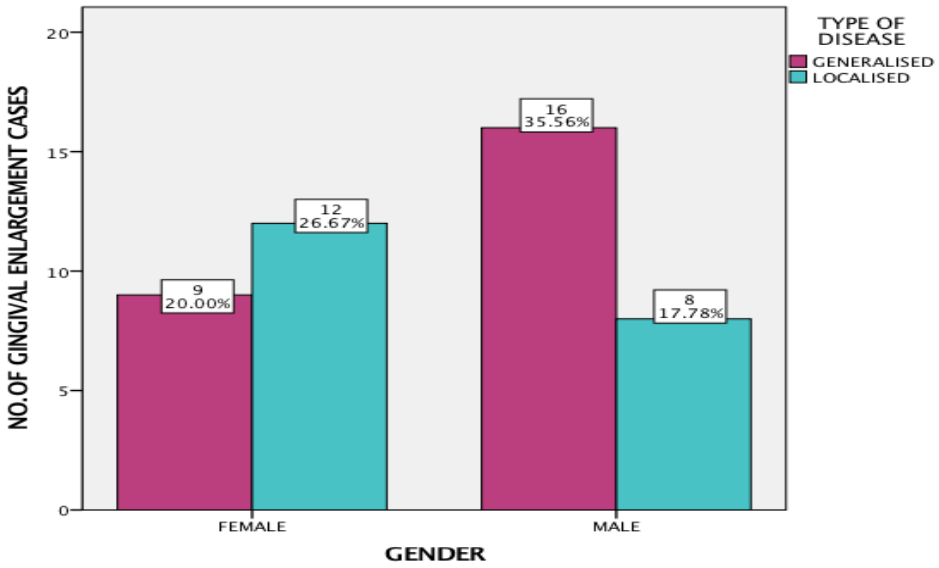

Figure 6 denotes the association between gender and type of disease [localised or generalised type of gingival enlargement.] X axis -gender of 45 patients and Y axis - number of cases with localised and generalised gingival enlargement among 45 patients. It can be estimated that among 45 patients who were diagnosed with drug induced gingival enlargement, 24 patients [males]and 21 patients [females]. Considering the type of disease, 25 patients [generalised] and 20 patients [localised] type of gingival enlargement. In the figure, colour blue[localised variant] and colour pink [generalised variant]. Chi square test was done and p value obtained was 0.096 it can be concluded that the chi-square test was not statistically significant.Based on this figure 6 it can be inferred that the majority of cases with drug induced gingival enlargement were males with predominantly generalised type of enlargement, but however the association was not statistically significant.

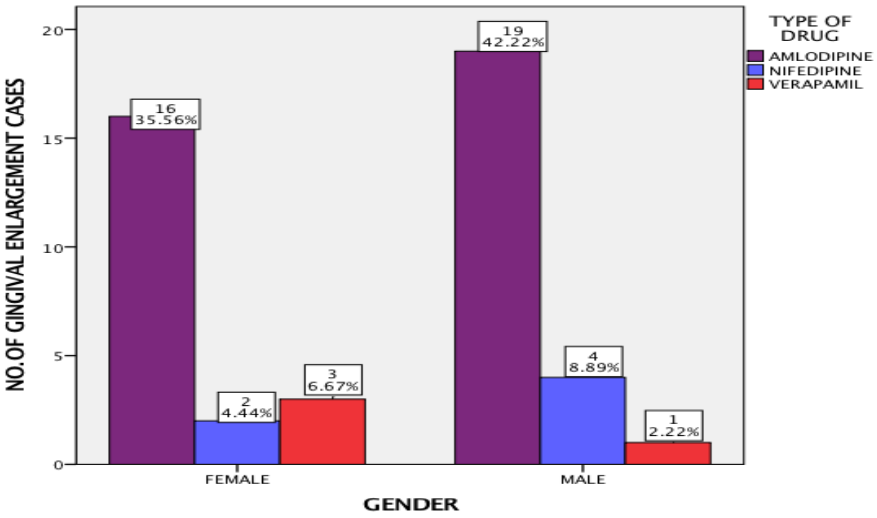

Figure 7 denotes the correlation between gender and type of drug used (amlodipine, nifedipine and verapamil.)X axis indicates the gender of patients and Y axis indicates the number of cases using the three types of drugs among 45 patients. In the figure, the colour purple denotes amlodipine[35], blue denotes nifedipine[6] and red denotes verapamil[4] induced gingival enlargement respectively. Chi square test was done and p value obtained was 0.421. Thus it can be concluded that the chi-square test was not statistically significant.Based on this figure 7 it can be inferred that the majority of cases with drug induced gingival enlargement were males with predominantly amlodipine induced enlargement, but however the association was not statistically significant.