A CROSS-SECTIONAL STUDY OF THE IMPACT OF ENDODONTIC INFECTIONS ON THE PATHOGENESIS OF CARDIOVASCULAR DISEASE

Dr. Zainbganayah Hasan Sulimani¹, Dr. Manal Abdulaziz Murad², Dr. Amal Mohammed Abushat³, Dr. Mohsen Daghustani⁴, Joud Nasir Bzaaid⁵, Malak Mohammed Al-Iraib⁶, Shahad Abid Alrehei⁷, Nahed Adel Saeedi⁸, Fatimah Tawfik Dahlawi⁹, Raghad Hassan Alsharif¹⁰, Abdulrahman Saeed Alharthi¹¹ and Dr. Hoda Jehad Abousada¹²

1. Consultant in restorative and implant Dentistry, Program director for Dental Implant Fellowship at Jeddah Specialty Dental Center.
2. Assistant professor of family medicine, Consultant Family Medicine, Family Medicine Department, King Abdulaziz University, Jeddah.
3. Consultant of orthodontics, SBO program director at KAU.
4. Consultant Endodontist.
5. General Dentist, Yasser Medical Center, Jeddah, KSA.
6. Dental Intern, King Khalid University, Abha, KSA.
7. Dentistry Program, Batterjee Medical College, KSA.
8. General Dentist, Adwaa Smile Medical Company, Jeddah, KSA.
9. General Dentist, Alqimmah Clinic, Khobar, KSA.
10. General Dentist, KFH, Madinah, KSA.
11. Dental Intern, King Khalid University, Abha, KSA.
12. Obstetrics and Gynecology Physician, King Fahad Armed Forces Hospital, Jeddah, KSA.

Introduction: The apical periodontitis possesses an association with the increased inflammatory markers’ levels, which contribute to the systematic immune response, leading towards systematic inflammation. The endodontic infections were reported to contribute to the CVD via the metastatic pathways; however, there is a requirement to analyse the impact of endodontic infections on the pathogenesis of the cardiovascular disease.

Aim: This research aims to assess the impact of endodontic infections on the pathogenesis of the cardiovascular disease.

Material and Method: This research was conducted using a cross-sectional research design by recruiting N=120 inpatients and outpatients visiting the healthcare organisation located in Saudi Arabia.

Results: The endodontic infections are likely to increase the overall inflammatory burden, which might increase the risk of CVD among the individuals. Due to the multifactorial aetiology of CVD, the oral diseases are perceived to possess associated with the CVD. The statistical analysis revealed that there is no association between the presence of the lesion of endodontic origin and cardiovascular diseases.

Conclusion: There is no association between the presence of the lesion of endodontic origin and cardiovascular diseases.
Introduction:-

The Cardiovascular Diseases (CVD) is a chronic inflammatory condition, which has been reported to possess an association with several risk factors, including age, gender, smoking, diabetes, high levels of cholesterol, smoking, and several other factors. However, there has been less focus on the potential contribution of the inflammatory processes towards CVD. With reference to the available evidence, the endodontic infections are common among individuals with CVD (Berlin-Broner et al., 2017). According to Gomes et al. (2016), the apical periodontitis possesses an association with the increased inflammatory markers’ levels, which contribute to the systematic immune response and lead towards systematic inflammation (GarG and Chaman, 2016). It has been reported that the older population are at an increased risk of developing endodontic infections, due to low levels of immunity, loss of hygiene, as well as lack of oral as well as dental care. The previously published evidence focused towards the investigation of the association between periodontitis and CVD reported a significant positive association between endodontic infections and CVD (Cotti et al. 2011; GarG and Chaman, 2016; Berlin-Broner et al., 2017). The older population with endodontic infections might not be necessarily present with CVD; however, the untreated tooth infections might predispose individuals to heart-related complications. Several authors have previously discussed the association between periodontitis and CVD; however, there is a gap in evidence regarding the association between periodontitis and CVD within the context of Saudi Arabia. This research aims to provide a significant insight regarding the association between periodontitis and CVD within the context of the population of Saudi Arabia.

Rationale:

Few of the researches have analyzed the association between dental caries with atherosclerosis, as well as risk factors associated with cardiometabolic complications, by considering a small percentage of the population (Petersen et al., 2014). However, the previously published studies lacked generalizability, and were vulnerable to the selection bias and. The previously published studies did not examine the association between the dental caries’ status, and CVD within the considered population sample (Kelishadi et al., 2010; Kim et al., 2019). Dental caries, and CVD both are the most common clinical complications, and are of public concern; therefore, the examination of the association between these clinical complications might facilitate in taking appropriate measures to reduce the potential risk of CVD due to periodontitis.

Literature Review:-

The cardiac complications contributed to more than 30% deaths across the globe in the year 2010 (Olvera Lopez et al., 2020). According to an estimate, by the year 2030, the non-communicable diseases are anticipated to account for more than three-quarters of the total rate of mortality worldwide. However, CVD alone will be accountable for a greater number of deaths within the low-income countries, as compared to the infectious diseases, including tuberculosis, malaria, HIV/AIDS, along with other diseases (Institute of Medicine, 2010).

The cardiac complications are likely to be prevented by focusing on the intake of a healthy diet, weight control strategies, physical exercises, and avoiding smoking. However, for managing the CVD complications, there is a requirement to take measures for preventing or treating oral infection (Berlin-Broner et al., 2017). The possible association between CVD, as well as chronic inflammatory processes of endodontic origin, have been reviewed by some of the researchers (Segura-Egea et al., 2015). The evidence had described the mechanism linking oral infections with the CVD and emphasized towards the role of oral pathogens (Cotti and Mercuro, 2015). The oral pathogen has contribution in the development of the endothelial dysfunction, fatty streaks formation, atherosclerotic plaques maturation, as well as increasing the predisposition towards rupture, resulting in vascular thrombosis (Kebschull et al., 2010; Janket et al., 2018). The endodontic infections were reported to contribute to the CVD via the metastatic pathways, including the spreading of endodontic infection via the transient bacteremia. These infections further result in metastatic injury due to the circulation of the endodontic microbial toxins, and the systemic inflammation, resulting from the immune response towards the endodontic pathogens (Gomes et al., 2013).

The evidence reported that apical periodontitis is likely to cause a local tissue response; however, the chronic periodontitis might not be and inclusively a local phenomenon, and might contribute to the systematic inflammation (Gomes et al., 2013; Brown et al., 2015; Cotti and Mercuro, 2015; Segura-Egea et al., 2015). The loss of tooth, which is referred to as the substitute measure of the history of the oral disease, was reported to possess an independent association with atherosclerosis, as well as early mortality (Gomes et al., 2012). In addition, the detailed
reviews had also addressed the biologic plausibility, along with the possible pathogenic mechanisms, including oral infections, CVD, as well as atherogenesis (Kebschull et al., 2010, Cotti et al., 2011, Janket et al., 2015). The observational researches also provided a significant insight that periodontal diseases are independently associated with atherosclerosis as well as CVD (Lockhart et al., 2012; Tonetti et al., 2013). However, the research conducted by Aminoshariae et al. (2018) proclaimed that the levels of evidence is low regarding the association between the presence of the lesion of endodontic origin and cardiovascular diseases. In this regard, with reference to the previously published studies, there are mixed opinions regarding the impact of endodontic infections on the pathogenesis of the cardiac complications, and further research is required to analyse the association.

**Research Question**
This research was conducted for answering the following research question.
What are the impacts of endodontic infections on the pathogenesis of cardiovascular disease?

**Aim:**
This research aims to assess the impact of Endodontic infections on the pathogenesis of the cardiovascular disease.

**Objectives:**
This research aims to fulfil the following research objectives.
1. To determine the age group most influenced by endodontic infections and the pathogenesis of the cardiovascular disease.
2. To validate a correlation between the effect of endodontic infections on cardiovascular patients.

**Method and Design:**
This research was conducted using a cross-sectional research design to assess the impact of endodontic infections on the pathogenesis of cardiovascular disease. According to Setia (2016), the cross-sectional research facilitates the researchers in measures the outcomes, as well as exposure among research participants at the same time. Moreover, Asiamah, Mends-Brew and Boison (2019) mentioned that the cross-sectional designs are utilised for the population-based surveys, and carrying out an assessment of the prevalence of clinical complications within the sample population. Thus, the cross-sectional research design was appropriate with reference to the research aims, which was the assessment of the impact of Endodontic infections on the pathogenesis of cardiovascular disease within the Saudi population.

**Research Settings and Population:**
This research was conducted within a healthcare organisation located in Saudi Arabia. The sample population for this research comprised of the inpatients and outpatients visiting the healthcare organisation. The sample population was recruited by using an inclusion and exclusion criteria, such that the inclusion criteria ascertained the inclusion of patients visiting the dental and cardiovascular departments of the healthcare organisations for a routine checkup. The patients visiting these departments of the healthcare organisation were contacted by the researchers and were invited in the research. The individuals willing to participate in the research were further briefed about the research-related details, and a total of N=120 individuals were selected for this research.

**Data Collection and Data Analysis:**
The data collection or this research was conducted by using a questionnaire focused on the assessment of the impact of endodontic infections on the pathogenesis of the cardiovascular disease. The consultant assessed the validity of the research questionnaire. The questionnaire comprised of the close-ended questions, and respondents were asked to return the filled questionnaires to the researchers.

The data analysis for this research was carried out by using the Statistical Package for the Social Sciences (SPSS). The statistical tests of descriptive statistics, as well as correlation analysis, were conducted for this research. The descriptive statistics determined the demographic factors, including age group, gender, as well as the nationality of the respondents. Moreover, the descriptive statistics also analysed the clinical complications experienced by the individuals after endodontic infections, along with the cardiovascular complications experienced by the population.

**Ethical Considerations:**
This research was conducted after acquiring ethical approval from the Institutional Review Board (IRB). The individuals willing to participate in the
research were included in the research, and informed consent was acquired from them, prior to participation. The research participants were allowed to withdraw from the research due to any reason, without any penalty. For protecting the individuals from the risk of harm, the responses from the filled questionnaires were entered into the software. Each response was coded by using a five-digit code for assuring the confidentiality of personal information of the respondents, and all responses were saved within a password-protected file. It was also assured to discard the data after completion of the research.

**Budget:**
This research was self-funded by the researcher.

**Results:**

**Demographics:**
Table 1 presented that the out of N=120 respondents, N=91 (75.8%) of the population was aged below 35 years. Whereas, N=21 (17.5%) of the population was aged between 35-45 years, and N=8 (6.7%) of the population was aged between 46-50 years.

**Table 1:** Age of Respondents.

| Age          | Frequency | Percent | Valid Percent | Cumulative Percent |
|--------------|-----------|---------|---------------|--------------------|
| Below 35 years | 91        | 75.8    | 75.8          | 75.8               |
| 35-45        | 21        | 17.5    | 17.5          | 93.3               |
| 46-50        | 8         | 6.7     | 6.7           | 100.0              |
| Total        | 120       | 100.0   | 100.0         |                    |

In addition, according to table 2, N=105 (87.5%) of the population was female, whereas, N=15 (12.5%) of the population was male. Table 3 presented the nationality of the respondents, and found that N=116 (96.7%) of the population were Saudi, whereas, N=4 (3.3%) of the population were non-Saudi.

**Table 2:** Gender of Respondents.

| Gender | Frequency | Percent | Valid Percent | Cumulative Percent |
|--------|-----------|---------|---------------|--------------------|
| Female | 105       | 87.5    | 87.5          | 87.5               |
| Male   | 15        | 12.5    | 12.5          | 100.0              |
| Total  | 120       | 100.0   | 100.0         |                    |

**Table 3:** Nationality of Respondents.

| Nationality | Frequency | Percent | Valid Percent | Cumulative Percent |
|-------------|-----------|---------|---------------|--------------------|
| Saudi       | 116       | 96.7    | 96.7          | 96.7               |
| Non-Saudi  | 4         | 3.3     | 3.3           | 100.0              |
| Total       | 120       | 100.0   | 100.0         |                    |

**Clinical Complications and CVD:**
The respondents were asked about the clinical complications experienced by them, and it was found that N=20 (16.7%) of the respondent experienced prolonged sensitivity, and pain due to hot and cold temperatures. In addition, N=15 (12.5%) of the respondent experienced swelling, as well as tenderness in the nearby gums, and N=14 (11.7%) of the respondents experienced severe tooth after chewing, or after the application of pressure (refer to table 4). Moreover, N=7 (5.8%) of the respondents experienced discoloration or darkening of the tooth, and an equal percentage of population, i.e. N=7 (5.8%) was reported to experience a persistent or recurring pimple on gums. In addition, a considerable percentage of the respondents, i.e., N=57 (47.5%) of the respondents did not experience any of the clinical complications.

The respondents were asked whether or not they had experience cardiovascular complications after experiencing endodontic infections. Table 5 presented that N=114 (95%) of the respondents denied to experience cardiovascular complications, whereas, N=6 (5%) of the respondents reported to experience cardiovascular complications.
Table 4: Complains Experienced by Respondents.

| Do you complain about one of the following problems? | Frequency | Percent | Valid Percent | Cumulative Percent |
|-----------------------------------------------------|-----------|---------|---------------|--------------------|
| Severe toothache pain upon chewing or application of pressure. | 14 | 11.7 | 11.7 | 11.7 |
| Prolonged sensitivity (pain) to hot or cold temperatures (after the heat or cold has been removed) | 20 | 16.7 | 16.7 | 28.3 |
| Discoloration (darkening) of the tooth. | 7 | 5.8 | 5.8 | 34.2 |
| Swelling and tenderness in nearby gums. | 15 | 12.5 | 12.5 | 46.7 |
| A persistent or recurring pimple on the gums. | 7 | 5.8 | 5.8 | 52.5 |
| I do not complain about anything from the above. | 57 | 47.5 | 47.5 | 100.0 |
| Total | 120 | 100.0 | 100.0 | |

Table 5: Complain of Cardiovascular Diseases.

| Correlations | Age | Gender | Nationality |
|--------------|-----|--------|-------------|
| Age          | Pearson Correlation | 1 | -.155** | -.018** |
|              | Sig. (2-tailed)     | .091 | .842 | |
|              | N                | 120 | 120 | 120 |
| Gender       | Pearson Correlation | -.155** | 1 | .351** |
|              | Sig. (2-tailed)     | .091 | .000 | |
|              | N                | 120 | 120 | 120 |
| Nationality  | Pearson Correlation | -.018** | .351** | 1 |
|              | Sig. (2-tailed)     | .842 | .000 | |
|              | N                | 120 | 120 | 120 |
| Do you complain about one of the following problems? | Pearson Correlation | .023 | -.013** | .168 |
|              | Sig. (2-tailed)     | .802 | .887 | .066 |
|              | N                | 120 | 120 | 120 |
| Do you complain of cardiovascular disease? | Pearson Correlation | -.075** | -.145** | .043 |
|              | Sig. (2-tailed)     | .418 | .115 | .644 |
|              | N                | 120 | 120 | 120 |

**. Correlation is significant at the 0.01 level (2-tailed).

Correlation between the Factors:

Table 6: Correlation between the Factors.

| Do you complain of cardiovascular disease? | Frequency | Percent | Valid Percent | Cumulative Percent |
|-------------------------------------------|-----------|---------|---------------|--------------------|
| Yes                                       | 6 | 5.0 | 5.0 | 5.0 |
| No                                        | 114 | 95.0 | 95.0 | 100.0 |
| Total                                     | 120 | 100.0 | 100.0 | |

Table 6 analyses the correlation or association between the considered variables by utilising the Pearson correlation coefficient. According to the Table 6, there is no significant correlation between the variables age, gender, and nationality with clinical complications experienced by the respondents, along with the complain of cardiovascular clinical complications. Table 6 presented a coefficient (r) value of 0.351 between the variables age and gender;
however, it did not provide insight regarding the association between endodontic infections and cardiovascular complications. Thus, it can be stated that there is no association between endodontic infections and cardiovascular complications within the sample of Saudi population.

Discussion:-
With reference to the evidence, the endodontic infections contribute to CVD via the metastatic pathways (Gomes et al., 2013). The analysis of clinical complications experienced by the individuals after between endodontic infections revealed that most of the individual experienced prolonged sensitivity, and pain due to hot and cold temperatures, swelling, as well as tenderness in the nearby gums, severe tooth after chewing, or after the application of pressure, and experienced discoloration or darkening of tooth, and persistent or recurring pimple on gums. Whereas, a considerable percentage of the sample population did not experience any clinical complication. In addition, a considerable majority of the total sample population did not experience CVD.

According to one of the evidences, the risk of CVD was significantly higher among the individuals with periodontal diseases, as compared to the individuals, who did not had experienced the periodontal diseases (Gomes et al., 2016). However, the evidence also reported that the oral diseases are primarily associated to the non-communicable chronic diseases via the common risk factors, including age, diet, lifestyle, smoking, low socioeconomic status, as well as a range of other factors (Brown et al., 2015; Gomes et al., 2016). The similar factors are likely to contribute to the CVD, which might give rise to the perception of association between the endodontic infections, and CVD. According to an evidence, after adjusting the risk factors, there might be weak association between oral diseases and CVD (Gomes et al., 2016). For this reason, it can be stated that the endodontic infections are likely to increase the overall inflammatory burden, which might increase the risk of CVD among the individuals (Segura-Egea et al., 2015). The total contribution of periodontal diseases to the CVD might be small; however, the clinical complications resulted due to the periodontal diseases are likely to increase the risk of deterioration of the risk factors associated to the CVD (Gomes et al., 2016). In this regard, due to the multifactorial aetiology of CVD, the oral diseases are perceived to possess association with the CVD. Another evidence revealed that the levels of evidence is low regarding the association between the presence of the lesion of endodontic origin and cardiovascular diseases (Aminoshariae et al., 2018). The presented research also validated the outcomes of research conducted by Aminoshariae et al. (2018), such that with reference to the outcomes of statistical tests considered within this research, there is no association between the endodontic diseases and CVD in the Saudi population.

Conclusion:-
In conclusion, it can be stated that the potential association between CVD, as well as chronic inflammatory processes of endodontic origin, have been reviewed by the researchers. With reference to the evidence, the apical periodontitis possesses an association with the increased levels of the inflammatory markers, which contribute to the systematic immune response and lead towards systematic inflammation. The individuals having low levels of immunity, loss of hygiene, as well as lack of oral as well as dental care are at an increased risk of developing endodontic infections, which put them at an increased risk of CVD. Thus, it is stated that the rate of prevalence of CVD has been increasing, and for managing the CVD complications, there is a requirement to take measures for preventing or treating oral infection.

With reference to the available evidence, the mechanism linking oral infections with the CVD, and emphasised towards the role of oral pathogens, which contribute to the development of the endothelial dysfunction, fatty streaks formation, atherosclerotic plaques maturation, as well as increasing the predisposition towards rupture, resulting in vascular thrombosis. The oral diseases are primarily associated with non-communicable chronic diseases via the common risk factors, including age, diet, lifestyle, smoking, low socioeconomic status, as well as a range of other factors. Almost similar factors are likely to contribute to the CVD. Thus, there is strong evidence regarding the association between the endodontic infections, and CVD. However, after adjusting the risk factors, there might be a weak association between oral diseases and CVD. With reference to the outcomes of statistical tests considered within this research, there is no association between the endodontic diseases and CVD in the Saudi population.

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