

EVALUATION OF FACTORS RESPONSIBLE FOR GANGRENE IN LOWER EXTREMITIES IN CASES OF PERIPHERAL ARTERIAL OCCLUSIVE DISEASE

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ABSTRACT:

Background: Peripheral Arterial Disease (PAD) is a slowly progressive atherosclerotic disease usually characterized by occlusion of lower limb arteries, ultimately causing acute or chronic limb ischemia. The PAD is largely under diagnosed and under treated because of unawareness of patients on claudication symptoms and present to the hospital at later stages with complications.

Study Design: The study design is of case series.

Aim of the Study: To study the various risk factors in terms of age, sex, occupation, pre-existing cardiovascular or metabolic diseases and other factors like smoking etc. involved in the development of gangrene in lower extremities.

To evaluate different clinical features of individuals with lower limb ischemia due to PAD.

Results: This study was done in the Department of General Surgery, Mamata General Hospital, Khammam, Telangana state from December 2018 to December 2020. A total number of 30 cases were included in this study, which satisfied the inclusion and exclusion criteria. The following conclusions were derived from the present study.

- Diabetes mellitus, hyperlipidemia, and hypertension are the modifiable risk factors for PAD. Patients at risk of developing PAD can be identified with regular monitoring of the risk factors and proper preventive medication and management.

- Medical treatment for preventing CV events in PAD subjects seems to be cost-effective. Among the evaluated treatment strategies, ACE-i displayed the largest reduction in event rates to the highest mean QALY. Aspirin treatment does not appear to be cost-effective due to the low reduction in event rates.

- Conclusion: Early diagnosis and treatment of PAD are critically important to reduce the risk of complications like gangrene in PAD and to minimize the risk of lower extremity amputations, risk of long-term disability, and to improve quality of life.

Key words: Peripheral Arterial Disease (PAD), Claudication, Gangrene.

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INTRODUCTION:

Peripheral Arterial Disease (PAD) is a slowly progressive atherosclerotic disease usually characterized by occlusion of lower limb arteries, ultimately causing acute or chronic limb ischemia[1]. Prevalence and incidence data typically show that peripheral arterial disease increases with age; is more common in men than women, and that symptomatic disease is only the tip of the iceberg[2]. In general, the prevalence of peripheral arterial disease is estimated to be fewer than 2% for men aged less than 50 years, increasing to over 5% in those aged more than 70 years[2]. Women reach these rates almost 10 years after men, although this gender difference decreases with increasing age. Poorer leg strength in women contributes to poorer lower extremity functioning in women with PAD than in men with PAD[3]. Several studies have shown that peripheral arterial disease correlates strongly with cigarette smoking. Other risk factors include hypertension, raised lipid levels (cholesterol and triglycerides for severe disease) and diabetes[3]. The incidence of non-fatal cardiovascular events appears to be higher in female PAD patients than in male PAD patients. Increased mortality risks are observed in both sexes, but total mortality is higher in male PAD patients[3].

In PAD, arterial blood flow to the lower extremities is reduced, leading to exertional skeletal muscle ischemia that results in significant discomfort (e.g., claudication pain) while walking even short distances. Claudication is the most recognized symptom of PAD. It typically commences shortly after walking begins and resolves only when the activity ceases and is classically described as an aching, cramping, painful or tired feeling in the calves[4]. Although claudication is considered the classic and hallmark symptom of PAD, only 7.5% of individuals report classic claudication as being part of their symptom experience[4]. Symptom reporting may differ based on disease severity, disease location, age or the presence of certain co-morbid conditions. Women may also have different PAD symptoms, since

PAD symptom definitions were based on male experiences and were established at a time when ischemic atherosclerotic diseases were thought to primarily affect men[5].

When individuals report symptoms that are not consistent with classic claudication, suspicion of disease presence is not triggered; therefore, individuals may not receive the necessary diagnostic testing and subsequent treatment for this chronic, debilitating disease. People suffering from PAD of different degree ranging from intermittent claudication to most severe critical limb ischemia may finally lead to gangrene[5].

The PAD is largely under diagnosed and under treated because of unawareness of patients on claudication symptoms and present to the hospital at later stages with complications[5]. Early diagnosis and treatment of PAD is critically important to reduce the risk of complications of like gangrene PAD and to minimise the risk of lower extremity amputations, risk of long-term disability and to improve quality of life. Even though many people suffer from PAD, only few will develop Gangrene. The present study was aimed to evaluate the risk factors responsible for development of lower limb gangrene in cases of PAD, so that appropriate risk reduction strategies can be applied to the high risk individuals to prevent the development of gangrene.

AIMS AND OBJECTIVES:

To study the various risk factors in terms of age, sex, occupation, pre-existing cardiovascular or metabolic diseases and other factors like smoking etc. involved in the development of gangrene in lower extremities.

To evaluate different clinical features of individuals with lower limb ischemia due to PAD.

METHODOLOGY:

This study was conducted in the department of General surgery, Mamata General Hospital, Khammam, Telangana state over a period of 24 months from October 2018 to September 2020. This study was conducted on 30 patients fulfilling the inclusion and exclusion criteria as mentioned below:

INCLUSION CRITERIA:

1. All cases of gangrene due to PAD involving lower extremities.
2. Both sexes with age>30years.
3. Patients willing to participate in the study.

EXCLUSION CRITERIA :

1. Patients with ulcer due to:

I. History of Trauma.

II. Raynaud's Disease

III. Syphilis

IV. Acute Embolism

V. Inflammatory arteritis

VI. SLE, Rheumatoid Arthritis

2. Patients unwilling to participate in the study.

DATA COLLECTION :

Patients admitted with gangrene involving toes or any part of lower extremity or both lower extremities fulfilling the exclusion and inclusion criteria were included in the study. ABPI < 0.9 was defines as PAD are involved. Institutional ethical committee (IEC) clearance was obtained, and informed written consent was taken from all the patients and were included in the study. Patients were subjected to thorough physical examination after taking detailed history. Relevant history including age, sex, and duration of the disease was noted. Relevant clinical examination including the examination of peripheral pulsations was carried out. Then all the patients were subjected to routine and special investigations which included:

1. Complete hemogram, renal function test.
2. ECG
3. Chest X-ray
4. Fasting and post prandial blood sugar, Glycosylated haemoglobin in case of diabetic patients
5. Lipid profile
6. Colour Doppler (Arterial) of the lower extremities.

Patients were treated by multi-modality treatment depending on the presentation. Medical management involved smoking cessation, administration of antiplatelet drugs like Aspirin and clopidogrel, use of statins to reduce hypercholesteremia and vasodilator drugs like cilostazole. Surgical management involved Dressing in case of ulcer and treating with appropriate antibiotics and culture report and amputation procedure done under due consents involving rays amputation, transmetatarsal amputation, below knee and above knee amputation in patients with gangrene of lower extremity.

A separate proforma for each patient, containing all the relevant particulars were maintained and data was entered Microsoft excel sheet for analysis at the end of the study.

OBSERVATIONS AND RESULTS:

The present study was an observational study conducted among the inpatients in the department of General Surgery diagnosed with gangrene of lower extremities due to peripheral arterial disease. Patients were selected as per the selection criteria. An analysis of various risk factors adjudged with the causation of peripheral arterial disease was done among them, and the results are obtained as follows.

1) AGE DISTRIBUTION:

The incidence of gangrene in PAD increases with advancing age. The peak incidence of disease in the age group of 61-70 years, which accounts for 36.6 % of the total population of the study.

2) SEX DISTRIBUTION:

Distribution of gangrene in PAD among the study population was more among men compared to women. The male to female ratio was 2.75:1.

3) EPIDEMIOLOGY:

The distribution of the study population according to demographic division was studied and most of the patients are from rural population that is 83.3%, and most of the patients are having no formal education that is 73.3%, The distribution of study population according to lifestyle was studied and results shows the most the patients with PAD are having sedentary lifestyle i.e., 70%.

4) RISK FACTORS FOR DEVELOPMENT OF GANGRENE IN PAD:

The incidence of gangrene in case of PAD was higher in diabetics in the present study. About 73% of study populations were known cases of diabetes mellitus. Hypertension was seen in 70% of the study population in the present study which was a risk factor for development of gangrene in PAD. 20% in the present study had a concomitant history of CAD along with PAD. 73% of the patients had hyperlipidaemia which is an another important modifiable risk factor that can be attributed to the pathogenesis of gangrene in case of PAD. The distribution of gangrene in case of PAD among smokers and non-smokers was studied, and results showed the incidence of gangrene in PAD was higher among smokers than non-smokers. Among the study population, 13.3% of patients had a history of CVA. The distribution of Peripheral neuropathy among the diabetic patients that is 22 patients in the study population which was 63.6% which was depicted in the table I

Table I: **RISK FACTORS FOR DEVELOPMENT OF GANGRENE IN PAD**

RISK FACTORS	NO. OF PATIENTS	PERCENTAGE%
Diabetic	22	73%
Non diabetic	8	27%
Hypertension	21	70%
Non-Hypertension	9	30%
CAD	6	20%
Non CAD	24	80%
Hyperlipidemia Present	22	73%

Hyperlipidemia Absent	8	27%
CVA	4	13.30%
Non-CVA	26	86.60%
Smoker	23	76.60%
Non Smoker	7	23.30%
Neuropathy Present	14	16.60%
Neuropathy Absent	8	36.30%

5) DISTRIBUTION OF INVOLVED ARTERIES:

Among the study population, the Dorsalis pedis artery was the most affected artery accounting for 90% of the cases.

6) DISTRIBUTION OF DISEASE ACCORDING TO ETIOLOGY:-

Among the study population, according to etiology Burgers disease was seen in 16.6% of patients as the age of 31-40 years of patients were smokers which is evident and atherosclerosis was seen in 83.3% of patients.

7) TYPE OF GANGRENE:-

Among the study population, Dry gangrene is seen in 66.6% of patients and wet gangrene is seen in 33.3% of patients.

8) DISTRIBUTION OF GANGRENE:-

Among the study population, gangrene at the level of toes was seen in 53.3% of patients followed by gangrene above ankle in 33.3% of patients.

9) PAIN CATEGORIZATION:-

Among the study population, rest pain which was seen in 70% of the patients of the patients followed by no rest pain which was seen in 30% of patients.

10) Local infection:-

Among the study population, local infection was seen in 70% of the patients with wet gangrene i.e., 10 patients.

11) MEDICATIONS TAKEN BY PATIENTS:-

Among the study population, medications used by the patients are 30% which is very low as compared to the patients not taken any medication which is 70% as depicted in table 13 and figure 11.

12) INVESTIGATIONS:-

a) ANKLE-BRACHIAL PRESSURE INDEX(ABPI):-

Following ABPI classification was used in the study [6]

>1.0 – Probably no arterial disease

0.9 – 0.99 – Borderline PAD

0.6 – 0.89 mild PAD

0.4 – 0.59 moderate PAD

<0.4 severe PAD [6].

Among the study population, 83.3% of patients are having the ABPI of severe level i.e., it is calculated by ABPI= Highest of systolic pressure of ankle / Highest of systolic pressure in both arms.

TABLE II: ANKLE-BRACHIAL PRESSURE INDEX

(ABPI) OF INVOLVED LIMB-ABPI	No. of patients	Percentage (%)
Moderate	5	16.6
Severe	25	83.3

b) DISTRIBUTION OF INVOLVED ARTERIES IN DUPLEX SCAN:-

Among the study population, the Dorsalis pedis artery was the most commonly affected artery accounting for 90% followed by Anterior Tibial artery (43.3%).

TABLE III : DISTRIBUTION OF INVOLVED ARTERIES IN DUPLEX SCAN

Artery with Monophasic flow	No. of patients (n=30)	Percentage (%)
Femoral Artery	0	0
Popliteal Artery	3	10
Anterior Tibial Artery	13	43.3
Posterior Tibial Artery	9	30
Dorsalis Pedis Artery	27	90

c) LIPID PROFILE:-

Lipid profile is another important investigation to rule out Hyperlipidemia which can be attributed to the pathogenesis of gangrene in case of PAD, in this study 73% of patients are having Hyperlipidemia. Low density lipoprotein is elevated in the 73% of the patients.

d) Blood picture:-

Among the study population, anemia was seen in 46.6% of the population and raised total leucocyte count was seen in 23.3%.

13) MEDICAL MANAGEMENT:-

Among the study population anti platelet drugs and statins are given for most of the patients (93.3%) as most of them are having atherosclerosis and hyperlipidemia. Flavunoids are secondary metabolites from plants and fungus which has anti-inflammatory and anti- oxidant effect and helps in decreasing atherosclerosis, so it was advised in 100% of patients. Anti-diabetic drugs are given in 73.3% of the patients.

14) TYPES OF AMPUTATIONS DONE FOR GANGRENE IN THE STUDY:

Depending on the level of involvement of the affected limb, amputation, or disarticulation was done. The most common procedure required was disarticulation of toes, done in 53.4% of the study population, followed by below-knee amputation (23.3%).

15) POST-OPERATIVE COMPLICATIONS:-

Among the study population wound healing with surgical site infection was seen in 26.6% of patients and wound healing without SSI was seen in 73.3% of patients.

DISCUSSION:

There is a global public health challenge of management of gangrene in PAD. The present study shows that PAD is common and almost one-fifth of elderly individuals have some stage of the disease which progress to gangrene. Intermittent claudication (IC) is probably under diagnosed and undertreated. It is that current prevention policies are not implemented efficiently. Though costs are associated with medication, our findings suggest beneficial effects for society and individuals of preventive drugs treatment for subjects with subclinical PAD.

PREVALENCE OF GANGRENE IN PAD:

Despite the abundance of epidemiological studies on gangrene in PAD, its true prevalence is not firmly established for all aspects of this disease. The results of the study indicate that PAD is common in the older age groups, and most subjects are asymptomatic. It is also probable that prevalence of gangrene in PAD will increase in less developed countries. According to WHO, CVD and PAD mortality rates in India, South Africa, and Brazil are 1.5-2 times higher than those in the US currently.

As the population ages, the prevalence of gangrene in PAD will dramatically increase. Moreover, as India's population is currently 1.3 billion, this means that there are already ~4 million people with PAD assuming the prevalence of PAD to be 6.3% (Premalatha et al., 2000)[7]. It is, therefore, crucial to understand the risk factors for gangrene in PAD in the Indian population.

Even if nothing changes in the next 30 years, population growth alone will lead to a major increase in CVD and PAD in developing countries, and it is concluded to be a "public health time bomb" if too little is done to reverse the trend. The numbers of patients with gangrene in PAD are likely to increase in the future. Alterations in risk factor occurrence may influence development. Achieving this is challenging for health care workers who need to commit to the development and implementation of policies for prevention.

EFFECT OF SEX AND PERCEPTION OF SYMPTOMS OF GANGRENE IN PAD

Sex hormones:

The protective effects of estrogens play a role in developing PAD. In the present study, there was male preponderance, which suggests that there is some protective role of female sex hormones in PAD. Increased arterial stiffness is found at an earlier age in men than women, and this may make them more prone to develop PAD in particular. After menopause, the process evolves in a similar way for women, and this may contribute to the later onset of CVD and PAD among women. It is possible that endogenous adaptation of the vasculature during the period of atherosclerosis progress is more efficient, and women, therefore, develop symptoms later in life and more often have subclinical disease.

Perception of symptoms:

There is other sex difference not necessarily related to disease manifestation and risk factors. Women perceive PAD symptoms differently from men when they eventually develop [8,9]. Older women with IC do not complain of leg symptoms because they accept walking difficulties as a part of the normal aging process. They also appear to seek medical care more scarcely than men. Women are more physically inactive and engaged in in-door household chores to a larger extent than men [10,11]. They, therefore, may have few demands on physical performance.

RISK FACTORS ASSOCIATED WITH GANGRENE IN PAD

Besides diagnosis issues and sex differences in disease patterns, risk factor occurrence is also important to consider. Not all PAD subjects have concomitant CV diseases and would thus remain unrecognized if PAD is not diagnosed. In fact, there might be a misconception that PAD always is associated with other CVD.

The present study included 30 patients irrespective of sex, presenting as gangrene of the lower limbs due to PAD, in the Department of General Surgery, Mamata General Hospital, Khammam, Telangana state over a period of 2 years from December 2018 to December 2020. The main objective of the study was to find out the various risk factors involved for PAD leading to gangrene in this geographical region. The various risk factors in this study are compared with that of the findings in other studies.

AGE:

Increasing age is a well-known risk factor for gangrene in PAD. Increasing age is the strongest determinant of PAD, CAD, and stroke. In the study, the most commonly affected age group was between 61-70 years, with 36.66%, followed by the age group between 71-80 years. Association of advanced chronological age with PAD is compared in this study. The results of this study are comparable with studies conducted by Nazir SavjiM et al [12], Janaka Weragoda et al [13] and Elizabeth Selvin et al [14] which shows similar results.

TABLE IV: COMPARISON OF PREVALENCE OF GANGRENE IN PAD WITH INCREASING AGE

Age (years)	Nazir Savji M et.al [12]	Janaka Weragoda et al [13]	Elizabeth Selvin et al [14]	Present study
30-40	6.7%	9.6%	11%	16.7%
40-50	2%	1.2%	1.7%	16%
51-60	3.5%	4.9%	5%	20%
61-70	7.1%	16.1%	9.5%	36.66%
71-80	13.0%	15.6%	20.5%	16.66%
81-90	22.3%	25.6%	28.7%	3.3%

SEX

Among the study population, 73.33% were males, and 26.67% were females. Males were more commonly affected in the present study. The results of this study are comparable to studies by Vogt et al [15], Natalia Egorova et al [16], and Elizabeth Selvin et al [14] which shows similar results.

TABLE V: COMPARISON OF PREVALENCE OF GANGRENE IN PAD IN RELATION TO SEX

Sex	Vogt et al [15]	Natalia Egorova et al [16]	Elizabeth Selvin et al [14]	Present Study
Male	72%	54%	46.2%	73.33%
Female	28%	46%	53.8%	26.67%
Total	100%	100%	100%	100%

EPIDEMIOLOGY:

The distribution of the population demographically was studied and ruled out that 73.3% of the patients are from rural areas and 26.6% of patients are from urban areas. Among the study population sedentary lifestyle was seen in 60% of the patients and patients with formal education was studied and rules out that 73.3% of patients are having No formal education and these results are compared with other studies Premlatha et.al [7], Janaka Weragoda et al [13], Briggitasigvant et.al [17], Dominic PJ et.al [18] which shows similar results.

TABLE VI : COMPARISON OF EPIDEMIOLOGY OF GANGRENE IN PAD WITH OTHER STUDIES

STUDY	RURAL AREA %	URBAN AREA%	SEDENTARY LIFESTYLE %	NO FORMAL EDUCATION
Premlatha et.al [7]	62%	38%	58%	70%
Janaka Weragoda et al [13]	68%	32%	61%	80%
Briggitasigvant et.al [17]	76%	24%	55%	75%
Dominic PJ et.al [18]	69%	31%	61%	69%
Present study	73.3%	26.6%	60%	73.3%

DIABETES MELLITUS:

Among the study population, the association between PAD and DM was seen in 73%, and results were compared with other studies. Diabetes mellitus was a major risk factor PAD in all the studies compared.

TABLE VII : COMPARISON OF DM AS A RISK FACTOR FOR GANGRENE IN PAD

Risk Factor	Briggita Sigvant et al [17]	Johansen et al [19]	Present Study
Diabetic	77%	57%	73%
Non-Diabetic	23%	43%	27%
Total	100%	100%	100%

According to a study by Nathaniel Clark, a classic history of claudication is less common. But, a patient may have subtle symptoms, like leg fatigue and slow velocity, and they attribute it to older age—diabetic patients with PAD experience worse lower- extremity function than those with PAD alone. Diabetic patients with PAD are more prone to the sudden ischemia of arterial thrombosis or neuroischemic ulceration or infection that rapidly results in an acute presentation with critical limb ischemia and risk of gangrene development, finally requiring an amputation.

By identifying a subclinical patient with the subclinical disease and instituting preventive measures, it may be possible to avoid acute limb-threatening ischemia and gangrene.

PERIPHERAL NEUROPATHY IN DIABETIC PATIENTS:-

The distribution of peripheral neuropathy in the study population was studied and seen in 63.6% and compared with other studies Premlatha et.al [7], Narres M et.al [21].

HYPERLIPIDEMIA:

In the present study, 73% of cases had hyperlipidemia. The status of patients at risk of developing gangrene in PAD in the present study is similar to that of studies by Briggisasigvant et.al (66% Patients have Hyperlipidemia) [17], Janaka Weragoda et al(73.86% Patients have Hyperlipidemia)[13], and Elizabeth Selvin et al (60.6% Patients have Hyperlipidemia) [14].

HYPERTENSION:

The association of HTN with PAD has been demonstrated in the present study. 70% of subjects had hypertension, and 30% had no hypertension. The present study showed a significant association between HTN and PAD. The results of this study are comparable with studies by Janaka Weragoda et al (78.41% patients has HTN) [13], and Elizabeth Selvin et al (73.6% patients has HTN) [14].

CORONARY ARTERY DISEASE:

The peripheral arterial disease of the lower limb coexists with other atherosclerotic disorders. Patients with PAD have a higher prevalence of coronary artery disease like myocardial ischemia, left ventricular dysfunction, aortic stenosis, ventricular systolic dysfunction, etc. In this study, 20% of patients had coexisting CAD and the results of this study are comparable with studies by Janaka Weragoda et al(15.91% patients has CAD) [13], and Elizabeth Selvin et al (24% patients has CAD) [14].

CVA:

Among the study population, 27% of patients had a history of CVA in the present study. 73% of patients had no history of CVA. The results of this study are comparable with studies by OXVASC (29.9% patients had CVA) [18], JanakaWeragoda et al (11.36% patients had CVA) [13], and Elizabeth Selvin et al (11.2% patients had CVA) [14].

SMOKING:

There are hypotheses proposed in the literature that smoking predisposes to PAD and CAD in different ways. One is the existence of a "threshold phenomenon in the pathogenesis of PAD. It implies that higher dosages of tobacco smoke are required to develop atherosclerosis in lower limbs than in the coronary circulation. On the other hand, there seems to be a sex difference in the sensitivity to tobacco exposure, as women seem to be more at risk than men. The same observation is also reported for CAD. In one study, for example, smoking increased the risk of CAD 6-fold for women but only 3-fold for men. Taking into account the increased sensitivity for female smoking and the changing smoking habits, smoking may induce PAD development in a sex-dependent manner. Among the subjects in the present study, 63% are smokers, and 37% are non-smokers. Results of the present study are comparable with studies by Briggisasigvant et al(59% are smokers) [17], Janaka Weragoda et al (44.32% are smokers) [14].

Drug prevention:

Providing those lifestyle modifications are implemented; there are some drug options to consider. Anti-platelet therapy (including aspirin and clopidogrel), statins, and anti-HTN drugs are considered in the treatment. Aspirin is considered the cornerstone of medical PAD treatment among most vascular surgeons and angiologists[22]. This is rather odd considering the lack of scientific evidence for its use

in this patient group. In fact, there is only one single randomized trial supporting its beneficial effects [23]. ACE-i and ARBs have shown clinical benefits independent of blood pressure lowering. Furthermore, it is possible that ACE-i treatment has a positive effect on walking distance in IC patients. These findings should be enough for promoting higher prescription rates of ACE-i for all PAD patients. Statins prevent CV events regardless of cholesterol values in high-risk CVD patients and improve leg symptoms in patients with IC and reduce rates of revascularization procedures. Population-level analyses suggest that secondary vascular protection could prevent more than 200,000 events in patients with PAD each year [24]. There are also available data of these drugs being cost effective.

In summary, the best treatment for PAD subjects consists of smoking cessation, physical exercise, and pharmacological prevention. Treatment with ACE-i and statins should probably be initiated in all PAD subjects. Evidence of the beneficial effects of aspirin seems to be ambiguous.

DIAGNOSIS OF GANGRENE IN PAD

Diagnosing the disease of interest correctly is extremely important in epidemiological studies, but this task has been proven difficult in PAD. This statement is not only valid for CLI (Chronic Limb ischemia), but also for APAD and IC (Intermittent claudication).

Ankle Brachial Pressure Index (ABPI)

The diagnostic tool for determining APAD, ABPI, is rather well-established, but some questions remain. One example is the controversy about whether to use the lower or, the higher ankle blood pressure from the two ankle arteries. The TASC document recommends the use of the highest ankle blood pressure, and American Heart Association guidelines do not specify whether to use the higher or lower of the two. In the present study, the highest ankle blood pressure was used, and there was an increase in the sensitivity to detect PAD, particularly APAD subjects [6]. It is well known that DM patients have falsely elevated ankle BP due to incompressible arteries, and thus likely to have ABIs > 0.9 and being categorized to not having PAD.

Numerous methods of calculating the ABI have been described based on variances in the numerator taken in the ABI equation. The current method recommended by the ACC/AHA involves using the higher of the two ankle systolic arterial pressures, termed high ankle pressure (HAP), as the numerator in the ABI equation. $ABPI = \text{Highest of systolic pressure of ankle} / \text{Highest of systolic pressure in both arms}$.

>1.0 – Probably no arterial disease

0.9 – 0.99 – Borderline PAD

0.6 – 0.89 mild PAD

0.4 – 0.59 moderate PAD

<0.4 severe PAD.

A second method reported in the literature, uses the lower of the two ankle systolic arterial pressures, termed low ankle pressure (LAP) as the numerator when calculating the ABPI. A calculation applied in some epidemiological studies uses the average of the two ankle systolic pressures as the numerator in the ABPI equation. A few studies have used the posterior tibial artery systolic pressure to calculate ABPI.

TREATMENT

Treatment of PAD consists of two main strategies. The first one aims to prevent CV events, and the second strives to relieve symptoms. CVD preventive measures, in addition to individual benefits, can

also reduce societal costs. The lack of cost-effectiveness data may contribute to this recommendation. Current treatment recommendations are as follows:

LIFESTYLEMODIFICATION

Smoking

As described previously, smoking is a proven strong risk factor for the development and deterioration of PAD [25]. Smoking cessation advice is, therefore, fundamental for PAD patients. Quitting smoking is very difficult for the patient with addiction seriousness at the same level as opiate dependency. Spontaneous cessations rates without intervention range from 2% to 5%, despite the fact that nearly 75% of smokers express a desire to stop. Behavioral interventions can improve these figures, but not much. Pharmacologic therapies are more effective than medical advice alone. Nicotine replacement strategies accomplish smoking termination rates between 11% and 34% at one year. Nicotine replacement is also cost-effective. There are other drugs that may improve cessation rates even further. One example is Bupropion, which is an “atypical” anti-depressive drug, with fairly high rates of smoking cessation compared to placebo. A newer drug, Vareniklin, is a

nicotine receptor agonist that has shown better results with good tolerability and low relapse rate.

Exercise Therapy:

Physical activity is a crucial factor in the success of both CVD and PAD patients. Studies indicate an inverse dose-response relationship between overall physical activity and the risk for PAD, which is linear at least up to a certain level of activity [26]. Exercise therapy also significantly improves walking ability in patients with IC. Most of these data come from trials employing supervised exercise programs consisting of 30-60 minutes exercises three times a week. An unsupervised exercise training program has substantial long-term benefits at a modest cost. A more expensive supervised exercise program is also cost-effective for most individuals with CVD and PAD.

The mechanisms behind its improvement capacity are proposed to include the optimized endothelial function and metabolic adaptation of the skeletal muscle. The development of collateral vessels with an improvement in blood flow may also contribute as well as more effective walking patterns.

Pharmacological treatment

PAD patients need effective medical care for an extended period of their lifetime. Therefore, different treatment modalities have to be carefully evaluated. Recommendations by different guidelines, separated by PAD stage.

Anti-platelet therapy

The positive effect of anti-platelet therapy is likely to act through several different mechanisms. Aspirin inhibits thrombosis formation by decreasing the production of prostaglandins and thromboxanes. Aspirin suppresses the production of these factors by irreversible inactivation of the cyclooxygenase enzyme [27]. Clopidogrel, a thienopyridine derivate, acts through different mechanisms. It blocks the activation of platelets by adenosine diphosphates, which selectively and irreversibly inhibits binding to its receptor on platelets and thereby inhibits platelet aggregation. Anti-platelet therapy is recommended to prevent associated CV morbidity and mortality in PAD. The use of aspirin is based on analogous data in CAD and stroke patients, where anti-platelet therapy has a documented efficacy. Anti-platelet therapy included aspirin as well as clopidogrel, ticlopidine, dipyridamole, and picotamide.

Lipid-lowering therapy

The positive effects of statins are numerous, and the action is not only mediated by its cholesterol-lowering ability. The main mechanism is inhibition of hydroxyl methylglutaryl coenzyme A reductase (HMG-CoA) that is the rate-limiting enzyme for cholesterol formation in the liver and other tissues. By inhibiting HMG-CoA reductase, statins reduce the hepatocyte cholesterol content, stimulate expression of LDL receptors, and ultimately enhance the removal of LDL from the circulation. Statins seem to stabilize plaques, so beneficial effects are reported, irrespective of change in LDL levels[27]. Triglyceride concentrations are reported to be reduced by 22%- 44% in patients with hypertriglyceridemia due to a decreased hepatic secretion of very-low-density lipoproteins. Statins further cause an increase in HDL with 5%-10%. The Heart Protection Study (HPS) provides evidence for the use of statins in patients with gangrene in PAD.

Simvastatin use was associated with a reduction of any vascular mortality, CAD events, and stroke. Its use also decreased non-coronary revascularizations by 17%, 24%, 27% and 16%, respectively. More recent data also suggests that PAD symptoms may be improved by statin treatment. Pain-free and total walking distance was also increased by statins in a study evaluating it against placebo. Guidelines suggest that all PAD patients (including APAD) should have an LDL cholesterol <2.59 mmol/L, and for subjects with other CV manifestations, the level should be <1.81mmol/L.

Anti-hypertensive treatment

Anti-HTN treatment prevents stroke and CAD. There are five major classes of anti-HTN agents; thiazide diuretics, β -blockers, calcium antagonists, angiotensin-converting enzyme inhibitors (ACE-i), and angiotensin-II receptor inhibitors (ARB). They have a different mechanism of action.

Thiazide diuretics decrease resistance in smooth muscle cells; β -blockers inhibit renin formation and decrease cardiac output. Treatment with calcium antagonists, ARB, and ACE-i will lead to dilatation of resistance vessels by separate mechanisms. Recent evidence suggests that the use of ACE-i in patients with PAD may offer protection against major CV events beyond those expected from only blood pressure lowering. These additional benefits may involve mechanisms such as reduction of oxidant stress, vascular, and cardiac muscle hypertrophy.

The Heart Outcome Prevention Evaluation study (HOPE) demonstrated that the primary endpoint of CV death or non-fatal MI or non-fatal stroke among APAD was reduced by ACE-i treatment with 14%-19%, depending on the level of ABI (clinical PAD 23%). In the past, β -blockers were avoided in patients with symptomatic PAD because of fears of vasoconstriction and deterioration of the peripheral arterial circulation. But a meta-analysis suggested that β -blockers do not adversely affect walking capacity[28]. One anti-HTN-drug, an alpha-blocker, caused improvement of PAD symptoms exemplified by an increased walking distance. Guidelines suggest that anti-HTN therapy should be administered to hypertensive PAD patients to achieve a goal of less than 140 mmHg systolic over 90 mm Hg diastolic or less than 130 mmHg systolic over 80 mmHg diastolic for diabetics and/or individuals with chronic renal disease.

SURGICAL TREATMENT:

About 53% of the study population required disarticulation of toes in the present study, followed by below-knee amputations. Various types of amputations in the study group of the present study are compared with a study by Narres M70.

TABLE VIII : COMPARISON OF VARIOUS TYPES OF AMPUTATIONS:

Type of amputation	The present study (%)	Narres M (%)
Toes	53.4	56
TMT	13.3	12
Lisfranc	0	2
Chopart	0	2
Syme	0	2
Below Knee	23.3	16
Above Knee	10	10

The Swedish Council on Technology Assessment in Health Care (SBU) recently performed a systematic literature review on this subject and found only two out of 1687 articles evaluating open revascularization in IC in a systematic and randomized way [29]. Surgical treatment increased walking capacity at the expense of some more complications in these studies. SBU concludes that there is some evidence for open revascularization for IC symptoms. Subjects with severe IC are willing to accept a substantial risk when it comes to surgical treatment, which is explained by the impaired health-related quality of life before treatment. According to SBU evidence, endovascular treatment of IC symptoms is inferior to open surgery, but despite the lack of data, it is often the first treatment choice in many vascular centers. The TASC document recommends that when choosing between techniques with equivalent short- and long-term clinical outcomes, the endovascular technique should be used first⁸⁰. Open revascularization has some indirect support for being effective. The rate of amputations was 15-20% after one year, compared to 40-50% in a placebo group in a study with CLI subjects not feasible for any kind of [30] revascularization [31]. CLI is afflicted with pronounced symptoms as rest pain and/or leg ulcers or gangrene with, consequently, low HRQL. For this patient group, any kind of reasonable revascularization is favored to avoid limb loss and relieve pain.

In summary, treatment in gangrene in PAD focuses on the prevention of CV risk and the relief of symptoms, for the former lifestyle modifications and smoking cessation are the cornerstones, along with drug treatment in some circumstances. Symptomatic relief can be achieved by revascularization, but its effect has limited scientific evidence behind it.

FUTURE ASPECTS:

There are obvious differences in the biology of men and women in the distribution of atherosclerosis and disease onset time. The influence of sex hormones like estrogen has been the main target for research in sex differences, but in particular, for peripheral manifestations of atherosclerosis, scientific evidence is still lacking. Future studies should be designed as a cohort follow-up study that evaluates the influence of risk factors and preventive interventions out of a gender perspective. ABI validity issues may also influence prevalence data for PAD. A study that clarifies sex differences in ABI measurements can be executed by performing several small methodological studies focusing on ABI levels in healthy men and women. Improvement is also needed in understanding the impact of PAD on functional capacity in older persons. PAD is suggested to accelerate the speed of functional decline¹²⁵. Studies indicate that men and women present IC symptoms differently, and women may be under diagnosed. Interesting future research should focus on the development of diagnostic tools for IC. Research on the benefits of risk factor modification and determination of the best medical treatment for

PAD patients with or without symptoms has lagged far behind, and a part of this is the lack of cost effectiveness analyses. Risk reduction would probably be equally beneficial in all PAD stages, and the diverging guideline recommendations for the prevention of CV risk in APAD subjects is a severe problem.

The WHO has defined screening as a medical investigation that does not arise from a patient's request for advice for specific symptoms or complaints⁸³. Understanding the spectrum of clinical pictures presented can be highlighted by the development of new questionnaires and interview questions covering IC symptoms. CVD prevention with drugs is an area that is largely underdeveloped in PAD. Future studies should be performed in PAD subjects only and enroll enough patients to enable evaluation of sex differences and the different PAD stages. The first studies should probably evaluate single treatment with target drugs to be followed by multiple drug strategies.

LIMITATIONS OF THE STUDY:-

The sample size in the present study is small (n=30).

It is an observational study

It is a Single institutional study.

CONCLUSIONS AND SUMMARY

This study was done in the Department of General Surgery, Mamata General Hospital, Khammam, Telangana state from December 2018 to December 2020. A total number of 30 cases were included in this study, which satisfied the inclusion and exclusion criteria. The following conclusions were derived from the present study.

- PAD is common in older age groups. The most commonly affected age group for development of gangrene was between 61-70 years, with 36.66%, followed by the age group between 71- 80 years, with 16.66% of the study population.
- Males (73.33%) are more commonly affected when compared to females.
- 73% of the study population had associated with DM which is an major risk factor development of gangrene.
- Among the study population, 73% of subjects had hyperlipidemia.
- Among the study population, 70% of subjects were hypertensive, and 30% of subjects were non-hypertensive.
- Among the study population, PVD and CAD were associated with only 20% of subjects, and the remaining 80% of subjects had no CAD.
- Almost 80% of the PAD subjects had no known cardiovascular disease and co-morbidity was associated with a more advanced stage of PDA.
- 63% of the study group had a history of smoking, and 37% of subjects had no smoking history which is an major risk factor for gangrene in PAD.
- Only a minority of subjects reported the use of the preventive drug, and men used it more frequently as compared to women.
- Diabetes mellitus, hyperlipidemia, and hypertension are the modifiable risk factors for PAD. Patients at risk of developing PAD can be identified with regular monitoring of the risk factors and proper preventive medication and management.

- Men and women with diagnosed IC appear to have the same disease and morbidity when objective measures of atherosclerosis in leg arteries such as ABI, DUS, and walking distance are employed. Women with IC report atypical symptoms more frequently than men.
- Medical treatment for preventing CV events in PAD subjects seems to be cost-effective. Among the evaluated treatment strategies, ACE-i displayed the largest reduction in event rates to the highest mean QALY. Aspirin treatment does not appear to be cost-effective due to the low reduction in event rates.
- Most of the patients are unaware of claudication symptoms and present to the hospital at later stages with complications.
- The results of our study suggest that early diagnosis and treatment of PAD are critically important to reduce the risk of complications like gangrene in PAD and to minimize the risk of lower extremity amputations, risk of long-term disability, and to improve quality of life.

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