



## CORONARY ARTERY ECTASIA; PREVALENCE AND CLINICAL CHARACTERISTICS: EXPERIENCE FROM A SINGLE CARDIAC CENTER

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**ABSTRACT... Background:** Coronary artery ectasia (CAE) is well-recognized but relatively uncommon finding during diagnostic coronary angiography. Coronary artery ectasia is defined as a segment of coronary artery that is 1.5 times more dilated in diameter than the nearby segments. Its clinical presentations are unstable angina, coronary vasospasm, and acute myocardial infarction. **Objectives:** To determine the clinical characteristics, presentation and treatment in patients with documented coronary artery ectasia in a single Cardiac Centre at Faisalabad City Pakistan. **Study Design:** Retrospective descriptive study. **Materials and Methods:** This was a single center retrospective, descriptive study. Patients of either gender with age 21-70 years who had coronary angiography at Faisalabad Institute of Cardiology Faisalabad were included in the study. Coronary angiograms performed from April 2013 to December 2016 were reviewed. Patients fulfilling inclusion and exclusion criteria were enrolled. Clinical and angiographic profiles of the patients having coronary ectasia were retrieved from hospital record. Clinical profile included: age, gender and cardiovascular risk factors. Angiographic profile; prevalence of coronary ectasia, type of ectasia, associated obstructive disease and coronary vessel involved were noted. **Results:** Total 22235 patients under went coronary angiography from April 2013 to December 2016 at Faisalabad Institute of Cardiology Faisalabad. Out of 22235, 16913(76%) were male and 5322(24%) were female. Coronary artery ectasia (CAE) was observed in 1044(4.7%). Out of 1044, 931(89%) were male and 113(10.9%) were female patients. Mean age of study population was  $49.5 \pm 11.8$  years. 368(31.97%) patients with CAE were in age group of 51-60 years followed by age group 41-50 years. 672 (64.36%) were hypertensive, 433 (41.7%) were diabetics, smoker were 574(54.98%). 442(42.33%) patients presented with ST elevation MI. 750 (71.84%) patient had mild Ectasia, 155 (34.87%) were suffering from severe coronary Ectasia. 364 (34.87%) patients had associated obstructive coronary artery disease. LAD was most commonly involved vessel in 392 (37.50%) followed by right coronary artery in 323 (30.94%). Type I ectasia was documented in 34.92%. **Conclusions:** In our study prevalence of CAE was 4.7%. CAE was more common in male, hypertensive, smokers and patients with Hyperlipedemia. Most common pattern of CAE was Type I and isolated ectasia without coronary artery obstruction. Left anterior descending artery was the most commonly involved vessel in ectasia followed by RCA.

**Key words:** Ectasia, Angina, Infarction, Coronary artery.

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## INTRODUCTION

Coronary artery ectasia (CAE) is relatively uncommon finding encountered during diagnostic coronary angiogram but it has been observed by cardiologists for more than two centuries.<sup>1-3</sup> CAE is documented in 3-8% of patients undergoing coronary angiography and in 0.22% to 1.4% of autopsy series. CAE is defined as inappropriate dilation of the coronary arteries exceeding the largest diameter of an adjacent normal vessel

more than 1.5 fold.<sup>1,4</sup> It can be either diffuse affecting the entire length of a coronary artery, or localized. The term ectasia refers to diffuse dilation of a coronary artery while focal dilation is known as coronary aneurysm.<sup>5</sup>

Several mechanisms are involved in the pathophysiology of CAE. In more than 50% of patients, most commonly CAE is related to atherosclerotic coronary artery disease (CAD)

and therefore it is also considered as a variant of coronary atherosclerosis. Atherosclerosis also explains the coexistent obstructive coronary artery disease (CAD) with coronary artery ectasia in the great majority of patients. However in 10% to 20% cases, CAE is related to inflammatory diseases.<sup>1</sup> In various studies it was documented that there is strong association of CAE with connective tissue disorders like scleroderma and Ehlers–Danlos syndrome.<sup>6</sup> Kawasaki disease, syphilitic aortitis and ANCA- related vasculitis was noted in patients with CAE.<sup>7</sup> CAE may be congenital in some patients. On IVUS it has confirmed that in coronary atherosclerosis arterial expansion and/or shrinkage can be manifestations. Conventional risk factors associated with atherosclerosis are also related with coronary artery ectasia.

The lesions in CAE have same characteristics as coronary artery atherosclerosis and some hypothesis links these both diseases. In some previous studies, pathological characteristics of CAE were described and it has features of chronic inflammation along with foam cells loaded with lipid deposition and loss of muscle wall elasticity.<sup>8</sup> The most probable mechanism that may involve in CAE is endothelium overstimulation by nitrous oxide (NO) or NO donors. In previous studies it was documented that NO production had increased via NOS pathway in CAE.<sup>9</sup>

Daugherty et al. documented in his study a strong relationship between angiotension II and ventricular remodeling.<sup>10</sup> Matrix metalloproteinase 2 is main enzyme which causes extracellular matrix degradation and play role in vascular remodeling. In patients with CAE, different studies have demonstrated an imbalance between metalloproteinase and endogenous tissue inhibitors.<sup>11</sup>

The Coronary artery ectasia produces sluggish blood flow in coronary vessels resulting in thrombus formation, vasospasm and spontaneous dissection leading to acute coronary syndrome. Regarding course of CAE, 15% patients have benign course, but features of old myocardial infarction were observed in 39% patients.<sup>1</sup>

The purpose of current study was to update about the prevalence of coronary artery ectasia along with its presentation, treatment options and to evaluate the clinical factors related to coronary ectasia and angiographic features of patients.

## MATERIALS AND METHODS

This study was conducted at Faisalabad Institute of Cardiology Faisalabad which is among the major tertiary care cardiac centers in Pakistan. We retrospectively analyzed coronary angiographies of all patients who were either admitted with ACS and their coronary angiography was performed or was referred to our center for angiography from other centers from April 2013 to December 2016 and subsequently CAE was diagnosed and who fulfill the inclusion and exclusion criteria. Coronary ectasia was defined as, dilation of coronary artery 1.5 times or more in diameter than the nearby segments in a part or whole of the coronary artery, with or without obstructive coronary artery disease.<sup>12</sup>

### Study Design

It was a single centre retrospective descriptive study.

### Sampling technique

Non-probability, purposive sampling technique was used

### Inclusion Criteria

Following patients were included in the study:

- Any patient of age 21-70 years of either gender.
- Patients with typical chest pain more than 20 minutes, ischemic in nature having unstable pattern, pain at rest, new onset of pain, increased severity or frequency of angina (accelerating angina).
- Patients with a diagnosis of ACS (ST elevation or non-ST) undergoing coronary angiography having CAE on final report.
- Fully assessable angiographic data.

### Exclusion Criteria

- Previous H/O PCI.
- H/O previous CABG.
- Patients with any valvular or structural heart

disease.

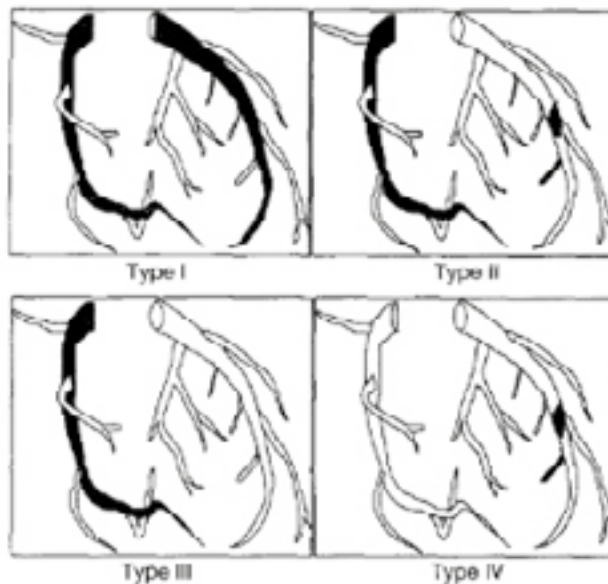
- Patients with cardiomyopathy.

Total 22235 patients attended Faisalabad Institute of Cardiology, Faisalabad for coronary angiography. They were either admitted with ACS or came with stable angina or were referred for angiography from other centers. Findings of 12 leads ECG of all patients were noted to observe any ST segment elevation or depression. Findings of transthoracic echocardiography were documented for any Valvular or structural heart disease. H/O risk factors for CAD like history of hypertension, diabetes mellitus, family H/O ischemic heart disease and hyperlipidemia was retrieved from the patient's record. Diabetes was identified on the basis of hospital record or if patient was taking anti diabetic medications (Insulin/ OHGA) or fasting blood sugar was  $\geq 126$  mg/ dl. Patient was labeled hypertensive on the basis of hospital record or if patient was taking antihypertensive medications or his/her BP was documented  $\geq 140/90$  mmHg in medical chart. Dyslipidemia was defined if total serum cholesterol was  $\geq 180$  mg/ dl in fasting state or patient was on statin therapy for it. In all patients who underwent angiography, Lab. investigations including complete blood count, fasting blood sugar, fasting lipid profile, blood urea and serum creatinine levels were noted from hospital data base. Values of cardiac markers (cardiac enzymes/ Troponin I level) were documented of each patient. Patients were considered smokers if still they were smoking (Huqa and/ or Cigarettes) at the time of angiography. Body mass index (BMI) was noted from the record. On the basis of ECG analysis and hospital record it was documented that whether the patient was admitted with ST/ non ST elevation ACS.

In all patients, Coronary angiography reports were reviewed by two independent observers for coronary ectasia or aneurysm along with any obstructive CAD. Left main stem disease was considered significant if stenosis was  $\geq 50\%$  and disease was considered significant if stenosis was  $\geq 70\%$  in other vessels. Markis classification of coronary artery ectasia was used to describe

the type of ectasia.

- |          |   |
|----------|---|
| Type I   | Involvement of two or more vessels in diffuse ectasia.                    |
| Type II  | If one vessel has diffuse Ectasia and other vessel has localized ectasia. |
| Type III | Involvement of only one vessel having diffuse ectasia.                    |
| Type IV  | If only one vessel is involved and has segmental or localized ectasia.    |



### STATISTICAL ANALYSIS

All the data was analyzed by SPSS (Statistical Package for Social Sciences) Version 23 for Windows. Categorical variables like gender, hypertension, Diabetes, hyperlipidemia, smoking, Troponin-I levels, cardiac enzymes and angiographic findings were documented by frequency and percentage and continues variables were presented as means  $\pm$ SD (Standard Deviation). Effect modifiers like age, genders, hypertension, diabetes, hyperlipidemia and smoking were stratified. To control its effect on outcome variable, post stratification chi-square test was applied. P value  $\leq 0.05$  was taken as significant. All tests applied were two tailed.

### RESULTS

Overall 22235 patients under went coronary angiography at our center from April 2013 to December 2016. 16913(76%) were male

and 5322(24%) were female. 1044(4.7%) had coronary ectasia (CAE), 931(89%) were male and 113(10.9%) were female patients. (Table-I). Mean age of study population was  $49.5 \pm 11.8$  years (range 21-70 years). Considering effect of age, maximum patients 368(31.97%) who were suffering from CAE were in age group 51-60 years followed by age group 41-50 years. Between age group 51-60 years, there were not only maximum sufferer in ectasia but disease was also more severe in this age group in 60(15.54%) patients followed by in age group 41-50, 44(13.37%) patients Table-II & IV. LAD and RCA were two vessels which were involved most commonly 137(35.49%) and 133(34.26%) respectively in disease in this age group Table IV. Only 2.2% patients having CAE were in age group of 21-30 years. 672 (64.36%) were hypertensive, 433 (41.7%) were diabetics, smoker were 574(54.98%) and dyslipidemia was documented in 514(49.23%) patients Table II & Figure-1. Family history for IHD was positive in 244(23.37%). Obesity was documented in 310(29.69%) patients. 641(61.39%) patients with ectasia had positive Trop I. 442(42.33%) presented with ST elevation MI, 286(27.39%) with non ST elevation MI, 142 (13.60%) came with unstable angina (Table-II).

	Patients	Male	Female
Overall patients	22235	16913(76%)	5322(24%)
Patients with Ectasia	1044	931(89%)	113(10.9%)

Table-I. Results of 4 years of coronary angiography.

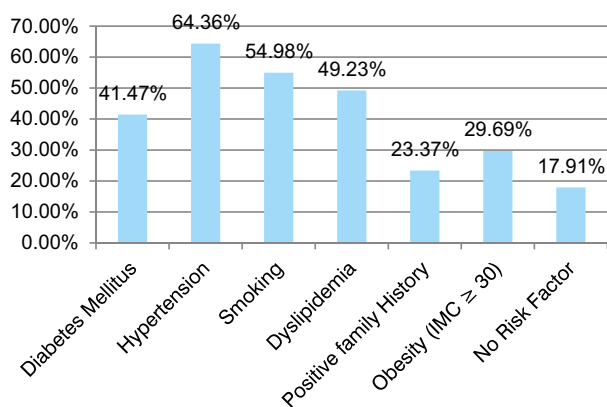


Figure-1. Risk factors for coronary ectasia

Characteristics	Number	Percentage
<b>Age (Years)</b>		
21-30	23	2.20 %
31-40	142	13.60%
41-50	329	31.51%
51-60	386	36.97%
61-70	164	15.70%
<b>Gender</b>		
Male	931	89%
Female	113	10.9%
Diabetes Mellitus	433	41.47%
Hypertension	672	64.36%
Smoking	574	54.98%
Dyslipidemia	514	49.23%
Positive family History	244	23.37%
Obesity (IMC $\geq$ 30)	310	29.69%
No Risk Factor	187	17.91%
Troponin I Positive	641	61.39%
<b>Mode of presentation</b>		
STEMI	442	42.33%
NSTEMI	286	27.39%
USA	142	13.60%
Others	174	16.66%
<b>ECTASIA</b>		
Mild	750	71.83%
Moderate	139	13.31%
Severe	155	14.84%
Ectasia with stenosis	364	34.86%
Ectasia without stenosis	680	65.13%
Type I Ectasia	365	34.96%
Type II Ectasia	299	28.63%
Type III Ectasia	215	20.60%
Type IV Ectasia	165	15.80%
Hospital Stay in Days(Mean) 5.31 days ( 5-9)		

Table-II. Baseline characteristics of patients

Vessel Involved	Number	Percentage
Left main coronary artery	29	2.78%
Right coronary artery	323	30.94%
Left anterior descending artery	392	37.55%
Left Circumflex artery	296	28.35%
Ramus Intermedius	4	0.38%

Table-III. Distribution of patients according to vessel involvement in ectasia

750 (71.84%) patient had mild Ectasia, 139 (13.31%) patient had moderate Ectasia, 155 (34.87%) were suffering from severe coronary Ectasia (Table-II). 364 (34.87%) patients had associated obstructive coronary artery disease.

Different Age Groups With Vessel Involved	Ectasia			Grand Total
	Mild	Moderate	Severe	
<b>21-30</b>	<b>15</b>	<b>4</b>	<b>4</b>	<b>23</b>
Left Anterior Descending Artery:	6	1	2	9
Left Circumflex Artery:	4	1		5
Left Main Stem	0	0	1	1
Right Coronary Artery:	5	2	1	8
<b>31-40</b>	<b>101</b>	<b>21</b>	<b>20</b>	<b>142</b>
Left Anterior Descending Artery:	42	11	7	60
Left Circumflex Artery:	29	5	5	39
Left Main Stem:	7	1		8
Right Coronary Artery:	23	4	7	35
<b>41-50</b>	<b>254</b>	<b>31</b>	<b>44</b>	<b>329</b>
Left Anterior Descending Artery:	100	10	16	126
Left Circumflex Artery:	79	7	8	94
Left Main Stem:	4	1		5
Ramus Intermedius:			1	1
Right Coronary Artery:	70	13	19	103
<b>51-60</b>	<b>263</b>	<b>63</b>	<b>60</b>	<b>386</b>
Left Anterior Descending Artery:	94	18	25	137
Left Circumflex Artery:	75	16	9	100
Left Main Stem:	9	2	2	13
Ramus Intermedius:	2		1	3
Right Coronary Artery:	83	27	23	133
<b>61 – 70</b>	<b>117</b>	<b>20</b>	<b>27</b>	<b>164</b>
Left Anterior Descending Artery:	47	5	8	60
Left Circumflex Artery:	39	7	11	57
Left Main Stem:	2			2
Right Coronary Artery:	29	8	8	45
<b>Grand Total</b>	<b>750</b>	<b>139</b>	<b>155</b>	<b>1044</b>

Table-IV. Ectasia in different age groups

Vessel Involved In CAE	Male	Female	Grand Total
Left Anterior Descending Artery	345	47	392
Right coronary artery	299	25	324
Left Circumflex Artery:	261	34	295
Left Main Stem:	23	6	29
Ramus Intermedius:	3	1	4
Grand Total	931	113	1044

Table-V. Correlation of ectasia with gender

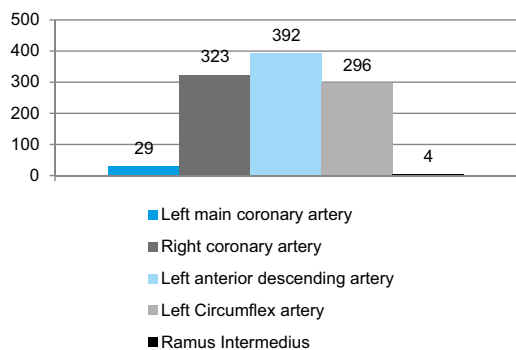


Figure-2. Coronary ectasia in different vessel

680 (65.1%) had no associated significant coronary artery disease. Regarding the types of ectasia, type I ectasia was most common and it was documented in 365(34.96%) while in 299 (28.63%) patient's type II ectasia was noted. In only 165(15.80%) patients type IV ectasia was documented (Table-II). Mean hospital stay was 5.1 days. In LAD ectasia was observed in 39 (37.50%) patients followed by right coronary artery 323 (30.94%), least involved vessel in coronary artery ectasia was Ramus Intermedius in 4 (0.387%) Table-III & Figure-2. Regarding effect

of gender on disease pattern, in male LAD was involved in 345(88%) and in 47(11.99%) female patients. In male, ectasia in RCA was observed in 299 (92.28%) and in female it was documented in 25(7.72%) Table-V.

## DISCUSSION

Coronary artery ectasia was documented by Morgagni for the first time.<sup>8</sup> Coronary artery ectasia (CAE) is a well-recognized but relatively uncommon finding encountered during coronary angiogram with various patterns of presentation and prevalence.<sup>1-3</sup> The gold standard investigation for the CAE remains the coronary angiogram.<sup>9</sup> Intravascular ultrasound is an excellent tool to assess luminal size and characterize arterial wall changes and it differentiates correctly a true from a false aneurysm caused by plaque rupture. Recently, MDCT is also used as a non-invasive tool for the diagnosis of CAE.

A lot of studies and analysis have been conducted with aim to understand this entity. Atherosclerosis remained the major etiological factor in adults while Kawasaki disease is the most common cause in children or young adults.<sup>13</sup> The specific causative mechanisms of abnormal dilatation of the lumen in CAE are essentially unknown. Current literature suggests that ectatic coronary arteries, even without the presence of coronary stenosis, are subject to thrombus formation, vasospasm, and spontaneous dissection. The prognosis of CAE depends directly on the severity of the concomitant coronary artery disease. CAE with obstructive coronary artery disease is a vicious condition because of its potential to cause several adverse cardiac events.

In our study prevalence of CAE was 4.7% which coincides with other international studies results. Leschka et al. conducted a study on 677 patients by using MDCT and he documented CAE in 3% of patients.<sup>14</sup> In other studies incidence of CAE was documented 0.3% - 4.9%.<sup>1-3</sup> It was documented in various studies that on the distribution of ectasia there is no any additional effect of age. Sharma et al found in his study that nature of ectasia in young and old patients was

not different.<sup>15</sup> Results of current study coincide with other international studies in that pattern of CAE is almost same in different age groups. In our study most of the patients belonged to age group of 51 - 60 years and this is same age group which is more prone to CAD. Higher incidence of CAE was observed in male than female in the largest series of patients in CASS registry by Swaye et al<sup>3</sup> and these results coincide with our results. Regarding risk factors for CAE, majority of the patients had same conventional major risk factors as were documented in patients with CAD having atherosclerosis which indicate that coronary ectasia is most commonly associated with atherosclerosis. Hypertension, smoking and dyslipidemia were the most common risk factors documented among patients of CAE in our study, however in different studies prevalence of different cardiovascular risk factors were different.<sup>3,16</sup>

It was documented in a previous study that in patients having familial hypercholesterolemia there is high incidence of CAE.<sup>17</sup> In current study dyslipidemia was observed in 514(49.23%) and hypertension was documented in 672(64.36%) and these results coincide with other studies.<sup>18</sup> It was described in various previous studies that there is a close association between aortic aneurysms and CEA.<sup>19</sup>

CAE is not a benign condition. Angina is the most common reported symptom of CAE,<sup>20</sup> but in other studies STEMI, non-STEMI, arrhythmias, or sudden death were reported.<sup>21</sup> In current study 442(42.33%) patients presented with AMI and only 142(13.60%) presented with UA. Regarding prognosis of patients with CAE the literature is unclear but in our study, only one patient death was reported (0.095%).

According to Tunick et al. study results, discrete ectasia develops exclusively in the presence of tight stenosis<sup>22</sup> but in our study 680(65.13%) patients had ectasia without significant co-existing stenosis. In current study type I ectasia was the most common pattern observed in our population. Demopoulos and H arikrishnan observed in their studies that RCA was the most

commonly involved vessel in ectasia followed by LCX and ectasia was observed in very little no of patients in LAD but in our study LAD was the main vessel involved in ectasia. In different previous studies it was observed that RCA showed diffuse nature of ectasia while it was of predominantly discrete form of ectasia in LAD<sup>23,24</sup> and our results coincide with these studies.

Regarding the management protocol for CAE, there are no guidelines; all the recommendations are on experience. In our study all the patients were treated with dual antiplatelets and statins but still there are questions for optimum treatment of ectasia, anticoagulants' like Warfarin, aspirin, calcium channel and beta-blockers all are suggested treatments.<sup>25</sup> To prove the treatment options for CAE, case-control studies must be carried out. Still there is some controversy regarding the use of oral anticoagulants for CAE. Oral anticoagulants were tested in a series of patients without any benefit in 2-5 years follow-ups<sup>23</sup>, so recommendation for anticoagulants must be reviewed in a larger cohorts study due to high risk of bleeding/hemorrhage with oral anticoagulants.

In our study most of the patients were discharged on DAP therapy (aspirin and clopidogrel). Use of beta-blockers and/or calcium channel blockers reduces the arterial flow so use of these drugs must be individualized for each patient. There are no specific recommendations for this strategy and the same applies to statins.<sup>26</sup>

## CONCLUSION

In our study prevalence of CAE was similar to other international studies reported in the medical literature. The main clinical presentation was acute coronary syndrome such as STEMI, NSTEMI and USA. CAE was more common in male, hypertensive, smokers and patients with Hyperlipedemia. Most common pattern of CAE was Type I and isolated ectasia without coronary artery obstruction. Left anterior descending artery was the most commonly involved vessel in ectasia followed by right coronary artery, left circumflex and left main coronary artery. In most of the cases

PCI was not feasible in the affected artery due to diameter of the vessel. After an acute event has been controlled in patients with CAE, still there is no consensus regarding ongoing management of this disease.

## STUDY LIMITATIONS

Our study was a retrospective single center study and there was no follow-up of patients. Secondly, our patient's record is not as good as international.

## ABBREVIATIONS

- **ACS:** acute coronary syndrome.
- **AMI:** acute myocardial infarction.
- **CAE:** coronary artery ectasia.
- **Cx:** circumflex artery.
- **iNOS:** inducible nitric oxide synthase.
- **LAD:** left anterior descending artery.
- **LMS:** left main Stem.
- **NO:** nitric oxide.
- **Non-STEMI:** Non-ST elevation myocardial infarction.
- **PCI:** Percutaneous coronary intervention.
- **RCA:** right coronary artery.
- **STEMI:** ST elevation myocardial infarction.
- **UA:** unstable angina.

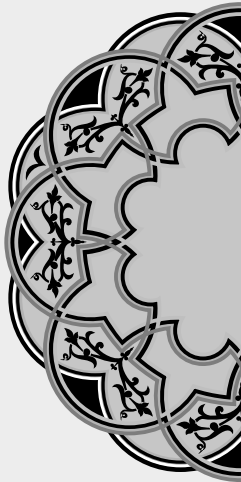
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*“You become what you believe.”*

**Unknown**

#### **AUTHORSHIP AND CONTRIBUTION DECLARATION**

<b>Sr. #</b>	<b>Author-s Full Name</b>	<b>Contribution to the paper</b>	<b>Author=s Signature</b>
1	<b>Dr. Liaqat Ali</b>	Data collection	
2	<b>Dr. Naeem Asghar</b>	Manuscript Writing	
3	<b>Dr. Muhammad Yasir</b>	Data analysis, manuscript writing	