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AUTHOR'S DECLARATION

I, **Dr. MADIHA MUSHTAQUE** hereby state that my MPhil thesis titled "**CHEST COMPUTED TOMOGRAPHY SCAN FINDINGS OF LUNG AND HEART SIZE AFTER COVID-19 PNEUMONIA**"is my own work and has not been submitted previously by me for taking any degree from this university, **The Bahria University** or anywhere else in the country/world.

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I, solemnly declare that research work presented in the thesis titled "**CHEST COMPUTED TOMOGRAPHY SCAN FINDINGS OF LUNG AND HEART SIZE AFTER COVID-19 PNEUMONIA**" is solely my research work with no significant contribution from any other person. Small contribution / help wherever taken has been duly acknowledged and that complete thesis has been written by me.

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Name of Scholar: Dr. MADIHA MUSHTAQUE

TO MY BELOVED PARENTS, HUSBAND AND KIDS

ACKNOWLEDGEMENTS

I would like to express my deepest and everlasting gratitude to Almighty Allah, as with His blessings this project is successfully completed.

I would like to express the deepest appreciation to my supervisor, Prof. Dr. Ambreen Usmani for her valuable advices, supports, ideas and continuous supervision in completing this MPhil research, since it was an impossible job for me to accomplish my dream without her. Hence, I pay my heartiest thanks to her.

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Finally, I wish to thank my family and spouse who have always encouraged me and supported to go on whenever I am devastated by difficulties in completing this study. They have shown their understanding and given advices for me to enhance my commitment in this research.
Thank you.

ABSTRACT

Over the past 2 years it has been known that coronaviruses cause respiratory illness in humans and also organ failure depending on what stage the illness is and if the patient is suffering from co-morbid diseases. The family of coronaviruses includes severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and the common cold. The new strain of coronavirus, COVID-19 which is highly contagious was first reported in 42 patients who were working in a sea food market in Wuhan, a city of China in December 2019. Since the 1st case report of coronavirus disease 2019 (COVID-19) in China December 2019, infection from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have spread promptly, causing a pandemic that has resulted in deaths of millions of people all over the world. Long-term effects of SARS-CoV-2 infection have become increasingly recognized on chest CT scan. Lung radiographic and CT scan changes are seen in convalescent COVID 19 patients which include permanent fibrotic like changes and they experience dry cough and fatigue even after 3 month of recovery.

Objectives were to assess pulmonary sequel and the risk factors for lung fibrosis on chest CT of survivors of severe COVID-19 pneumonia. To assess the difference in lung sizes of COVID-19 survivor and normal individual on CT scan of chest. To assess the difference in heart size of COVID 19 survivor and normal individual on CT scan of chest.To assess the displacement of hilum of lung due to fibrosis on chest CT scan. To assess pulmonary function test of COVID 19 survivors on Spirometery.

Eighty four subjects enrolled in the study; 42 (cases) survivors of COVID 19 and 42 (controls) without COVID 19.

Research was carried out in PNS Shifa hospital radiology department. Eighty four cases and controls underwent chest CT scan. Demographic details were taken and lungs and heart sizes measured using ruler in millimeters. All the data entered on a predefined proforma.

Result showed the significant decrease in diameters of the lungs of survivors of COVID-19 pneumonia as compared to the controls with significant p-value. The diameters of heart were increased on chest CT scan in COVID 19 survivors then the

healthy individuals and significant results found. COVID 19 patients with hypertension or smoking habits require more ICU admission and oxygen support. In conclusion COVID 19 disease causes injury to lungs and heart and fibrosis may persist for longer duration. Follow up of such patients are necessary at 3, 6 and 12 months and other parameter should be investigated like lung function test, cardiac enzymes and echocardiography.

Key Words: COVID 19, CT scan, fibrotic changes, PFT, Spirometry, Cardiac enzymes, Echocardiography

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LIST OF ABBREVIATION

COVID-19	Corona Virus Disease
HRCT	High Resonance Computed Tomography
CT	Computed Tomography
RT-PCR	Real Time Polymerase Chain Reaction
SARS	Severe Acute Respiratory Syndrome
WHO	World Health Organization
GGO	Ground-Glass Opacity
ICU	Intensive care unit
SPO2	Pressure of oxygen
CMR	Cardiovascular Magnetic Resonance

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CHAPTER 1

INTRODUCTION

1.1 BACKGROUND

In December 2019, 42 patients reported with cough and dyspnea in the city hospital of Wuhan, China. These patients were declared infected with severe acute respiratory syndrome (SARS) and later this disease was termed as Coronavirus disease COVID 19. It was a very contagious disease and it became a pandemic in 3 months of first case reported and World Health Organization (WHO) declared COVID 19 as global health emergency in March 2020. (Wang et al., 2020) The disease progression of COVID-19 ranges from mild symptoms and signs of acute upper respiratory tract infection, to severe pneumonia and failure of respiration in severe cases along with septic shock. COVID-19 cases are also reported without any illness (Barisione et al., 2020).

Lungs are primarily involved in COVID 19 pneumonia. Some cases were reported with atherosclerosis and heart failure after the infection. Due to the vast COVID-19 clinical spectrum, a lot of challenges faced by the clinical staff on frontline stretched resources prioritization as well as prediction of prognosis. Thus, there is a critical prerequisite of risk analysis for management and treatment. The major risk factors for death are comorbidities and older age. (Zhao et al., 2020)

The Corona virus is diagnosed by the real-time reverse-transcription–polymerase-chain-reaction (RT-PCR) assay through nasopharyngeal and oropharyngeal

swab samples. RT-PCR assay is the standard for diagnosis of coronavirus disease. At the period of initial presentation 30-60% was the total positive rate of RT-PCR.

Major draw backs of this test are that false-negative rate are high and availability was also limited during the outbreak of disease. (Cinkooglu et al., 2020)

Molecular biological testing and imaging are currently scientific interest for diagnosis of disease. One of the major queries is about the chest CT in screening and diagnostic process in contrast with real-time polymerase chain reaction (RT-PCR) test that is why we do not do PCR just take CT Scan (Kovacs et al., 2020)

CT scan chest plays a crucial role in the analysis and management of COVID-19 pneumonia. Some studies revealed diverse CT results, with main abnormalities including consolidation and ground glass opacities. Accurate diagnosis and disease staging can be better understood by CT scan findings of patient of coronavirus disease. Infiltration and distribution patterns among lobes of lungs and infiltration are more prominent in CT scan findings that provide information related to diagnosis. Characterization of COVID-19 pneumonia is done by distribution pattern of the lesion. Most of the patients had peripheral, subpleural and bilateral lung involvement (Wang et al., 2020)

1.2 GROSS ANATOMY OF LUNGS

The major organs of the respiratory system are the lungs. The right lung is slightly larger than the left lung and divided into sections, or lobes. The right lung has three lobes and left lung has two lobes. The lungs are situated in the thorax separated by narrow median space called mediastinum, which also includes the heart, trachea, esophagus, and many lymph nodes. The external covering of lungs known as pleura protects the lungs and the muscular diaphragm separate the lungs from abdominal cavity. The lungs are roughly cone shaped with three surfaces and three borders, apex and base. Due to the presence of the heart the left lung is slightly smaller than right lung. The upward projection of lungs above the 1st rib and into the root of the neck is known as apex. The lung’s inferior surface which sits on the diaphragm is known as base. (Sinnatamby, 2012)(Figure 1.1)

1.2.1 Lobes

The right lung is divided into three lobes superior, middle and inferior by oblique and horizontal fissures. The left lung divided into two lobes superior and inferior by an oblique fissure. (Wineski, 2012)

1.2.2 Surfaces

There are three surfaces of lungs, which corresponding to the thoracic area. The mediastinal surface of the lung faces the lateral aspect of the middle mediastinum. The lung hilum (where structures enter and leave the lung) is located on this surface. The base of the lung is formed by the diaphragmatic surface. It rests on the dome of the diaphragm, and has a concave shape. This concavity is deeper in the right lung, due to the higher position of the right dome overlying the liver. The costal surface is smooth and convex. It faces the internal surface of the chest wall. It is related to the costal pleura, which separates it from the ribs and innermost intercostal muscles. (Figure 1.2) (Moore, Daley &Agur, 2014)

1.2.3 Borders

The anterior border of the lung is formed by the convergence of the mediastinal and costal surfaces. On the left lung, the anterior border is marked by a deep notch, created by apex of the heart. This t is known as the cardiac notch. The inferior border separates the base of the lung from the costal and mediastinal surfaces. The posterior border is smooth and rounded (in contrast to the anterior and inferior borders, which are sharp). This is formed by the costal and mediastinal surfaces meeting posteriorly (Figure 1.2) (Moore et al., 2014)

1.2.4 Root and Hilum

The lung root is a collection of structures that suspends the lung from the mediastinum. Each root contains a bronchus, pulmonary artery, two pulmonary veins, bronchial vessels, pulmonary plexus of nerves and lymphatic vessels as shown in (Figure 1.3). All these structures enter or leave the lung via the hilum a wedge shaped area on its mediastinal surface. (Fig 1.3) (Moore et al., 2014)

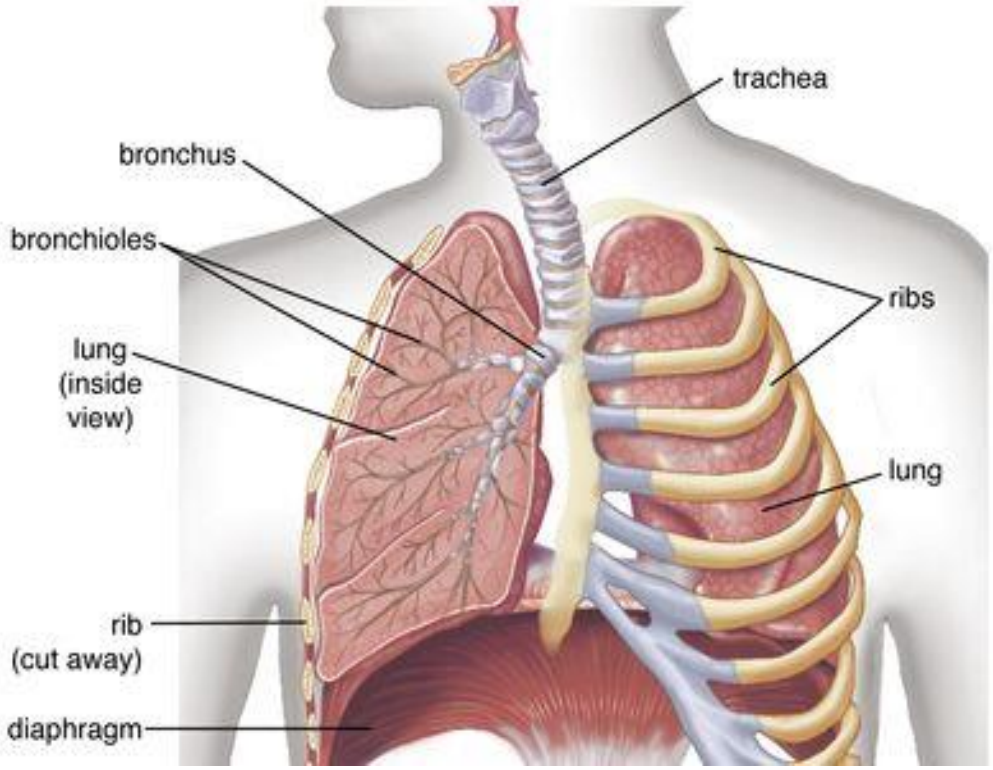


Figure 1.1: Anatomy of lungs (Britannica.com)

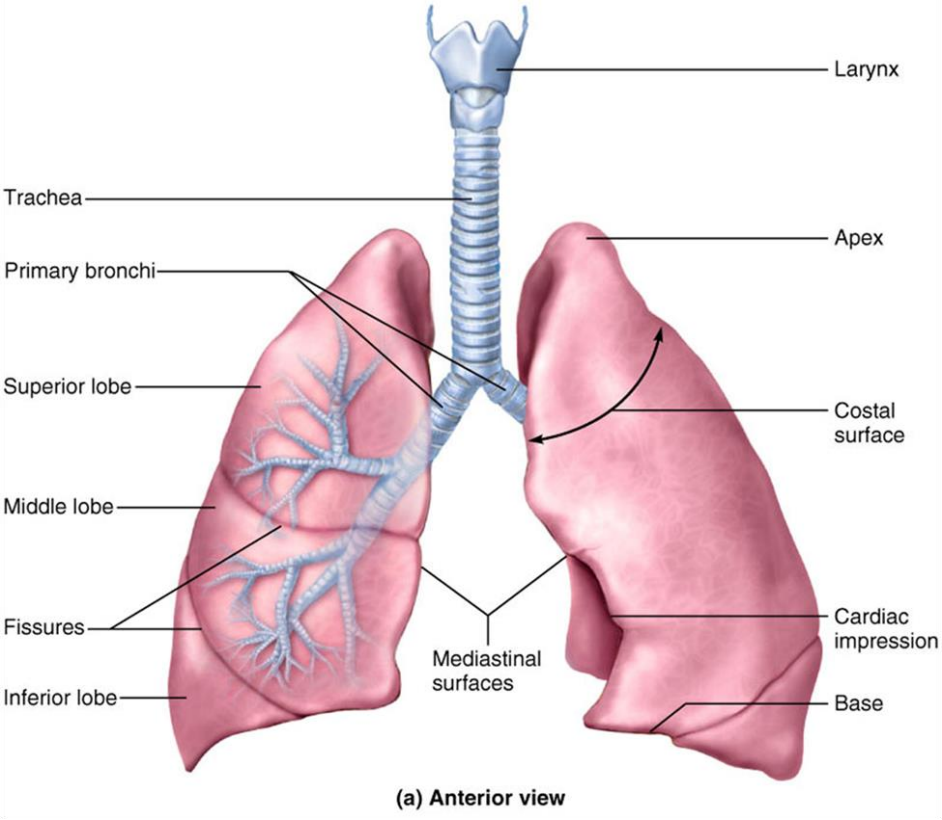


Figure 1. 2: Lobes and surfaces of the lungs (Netters, 2010)

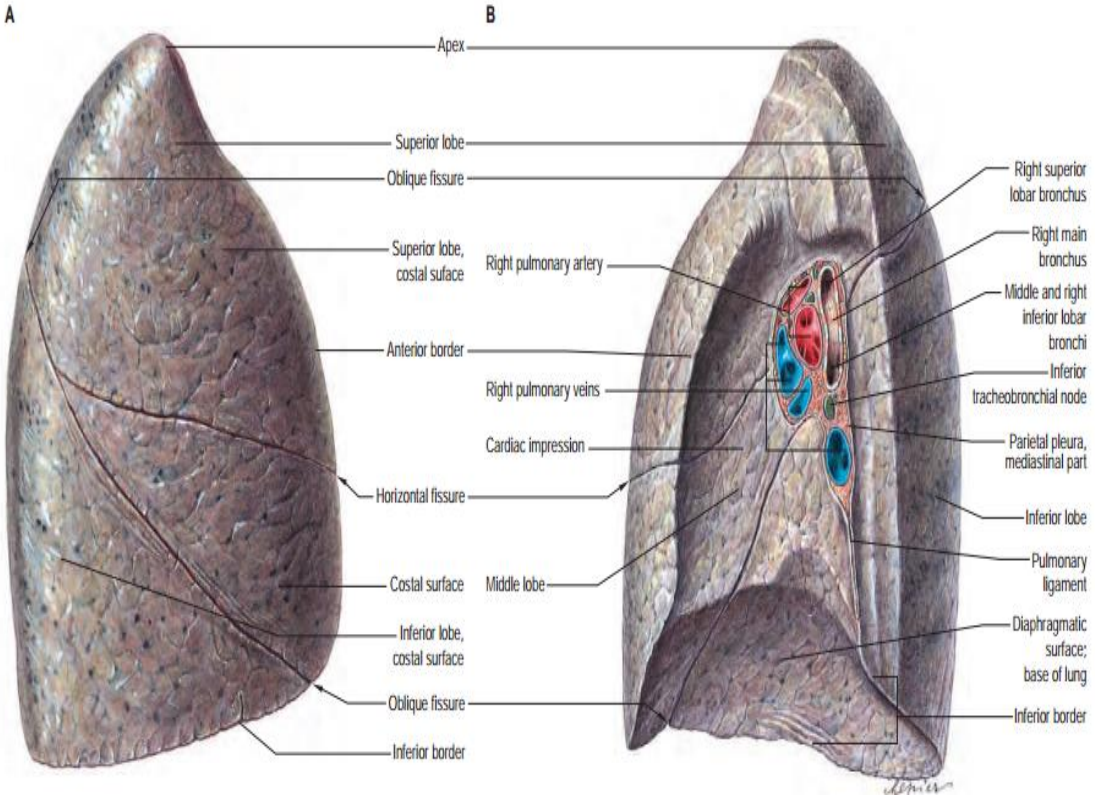


Figure 1.3: Lateral and medial surfaces of Right Lung (Moore et al, 2020)

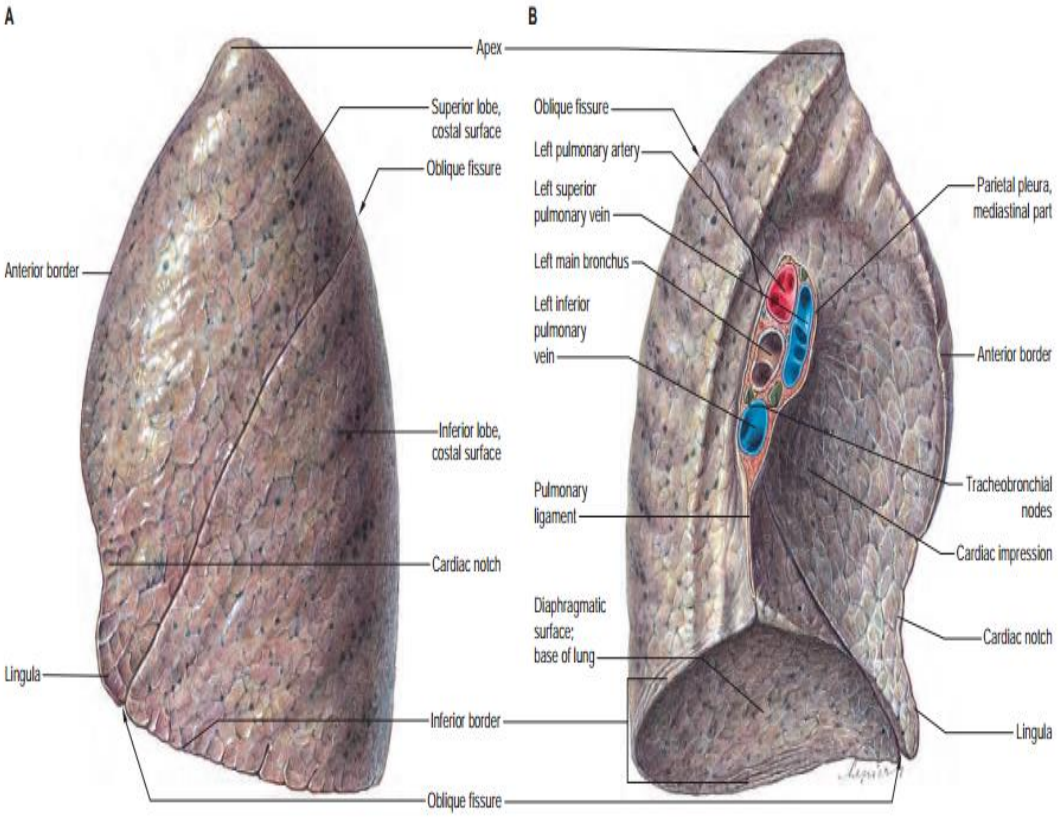


Figure 1.4: Lateral and medial surfaces of Left Lung (Moore et al, 2020)

1.3 BRONCHIAL TREE

The bronchial tree is a series of passages that supplies air to the alveoli of the lungs. It begins with the trachea, which divides into a left and right bronchus (Snell, 2012).

Each bronchus enters the root of the lung, passing through the hilum. Inside the lung, they divide to form lobar bronchi one supplying each lobe. Each lobar bronchus then further divides into several tertiary segmental bronchi. Each segmental bronchus provides air to a bronchopulmonary segment. These are the functional units of the lungs. The segmental bronchi give rise to many conducting bronchioles, which eventually lead into terminal bronchioles (Figure 1.4) each terminal bronchiole gives off respiratory bronchioles, which feature thin walled outpocketings that extend from their lumens. These are the alveoli the site of gaseous exchange. (Snell, 2012)

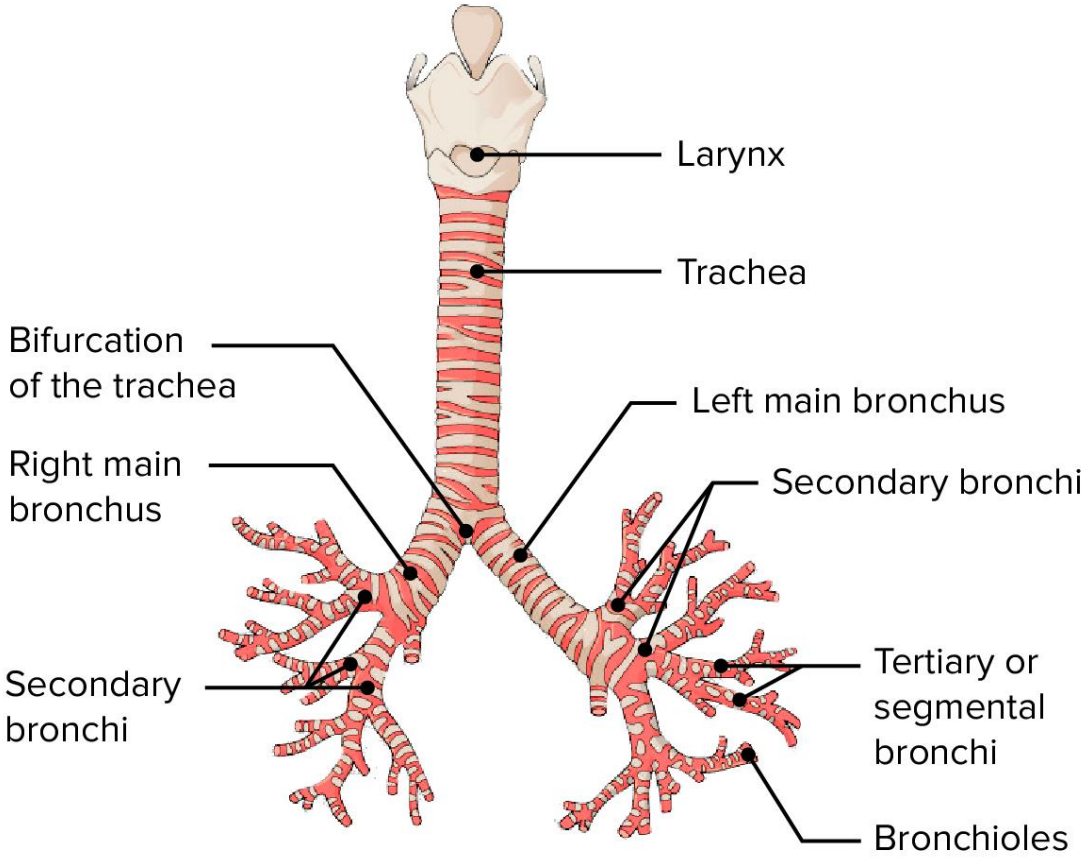


Figure 1.5 Bronchial tree (Snell, 2012)

1.4 BRONCHOPULMONARY SEGMENTS

The continuous demands of oxygen by every cell within the human body and the constant need to remove waste gases like carbon dioxide are met by the lungs. These paired organs assume their role as the gas exchange organs with the first cry of the new born and continue working until the end of life. While the functional unit is the capillary-alveoli interface, the lung is divided into segments. The bronchopulmonary segments are the largest functional divisions of the anatomical lobes; each receiving their own air and blood supply (Figure 1.7, Figure 1.8) There are ten bronchopulmonary segments located within the right lung, (Figure 1.7) and 8 – 9 on the left side as some of the segments may fuse together (Figure 1.8) Each bronchopulmonary segment is served by corresponding branches of the bronchial tree, along with their own arterial supply. However, the venous and lymphatic vessels pass through the intervening septa that separate the segments from each other (i.e. within the intersegment planes). The segments are separated from each other by bands of connective tissue. As a result, each bronchopulmonary segment is functionally separate from the adjacent segments. Aside from the pulmonary fissures, there are no superficial anatomical markings that facilitate identification of the bronchopulmonary segments. The superior lobe of the right lung has three bronchopulmonary segments the apical, anterior and posterior. The middle lobe of the right lung lies between the horizontal (superiorly) and the anteroinferior part of the oblique fissures (inferiorly). It is subdivided into lateral and medial bronchopulmonary segments. The lateral segment is best represented on the costal surface of the lung, while the superficial boundary of the medial segment wraps around the anterior border of the lung. (Moore et al., 2020)

The inferior lobe of the right lung has five bronchopulmonary segments. The superior segment is represented on both the costal and mediastinal surfaces of the right lung; as the segment also includes a portion of the posterior border of the right lung. The medial basal segment is best represented on the mediastinal surface of the lung, as it lies below the hilum. It is anteriorly related to the posterior basal segment, which abuts the lateral basal segment around the posterior border of the lung. The anterior basal segment is limited anteriorly by the caudal part of the oblique fissure and is juxtaposed with the lateral basal segment posteriorly. (Moore et al., 2020)

Although there are only two lobes in the left lung, there is some symmetry among the bronchopulmonary segments bilaterally. However, some segments of the left lung merge. Consequently, there are fewer bronchopulmonary segments on the left than there are on the right. The superior lobe of the left lung contains four bronchopulmonary segments. The apicoposterior segment represents the fusion of the apical and posterior segments. It is limited poster inferiorly by the superior aspect of the left oblique fissure and is adjacent to the anterior segment of the superior lobe. Although the lingular lobe of the left lung is considered a part of the superior lobe, it is analogous to the middle lobe of the right lung. Similarly, it is divided into two bronchopulmonary segments, namely the superior and inferior lingular segments. The superior lingular segment is located between the caudal boundary of the anterior segment and the superior boundary of the inferior lingular segment. Both are anterior to the hilum of the left lung, and the inferior segment is limited inferiorly by the inferior half of the oblique fissure (Fig 1.4) (Standring et al., 2016)

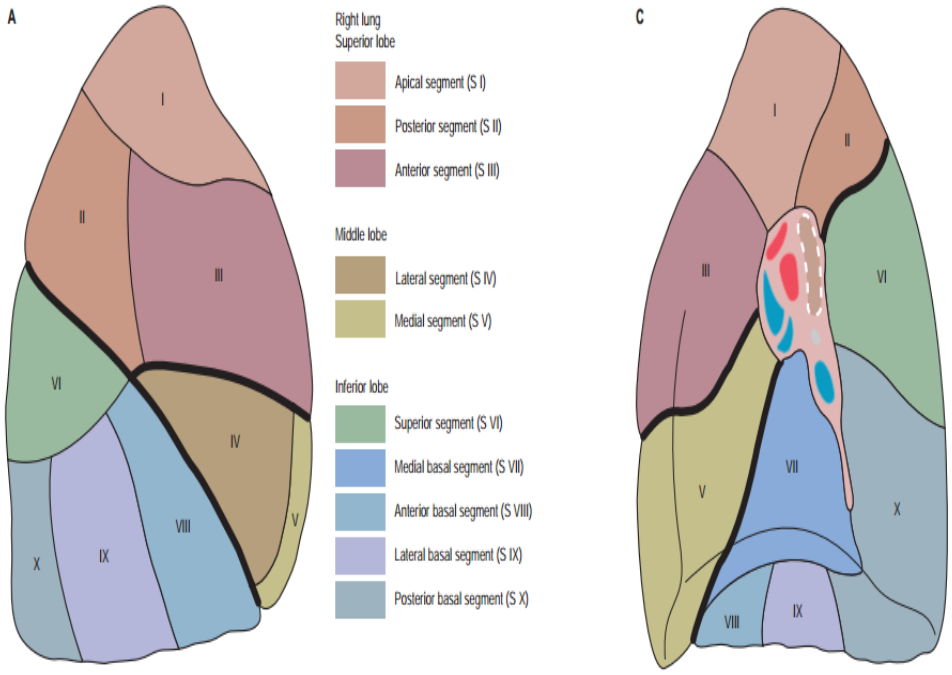


Fig 1.6 Bronchopulmonary segment of Right Lung

(Netter, 2010)

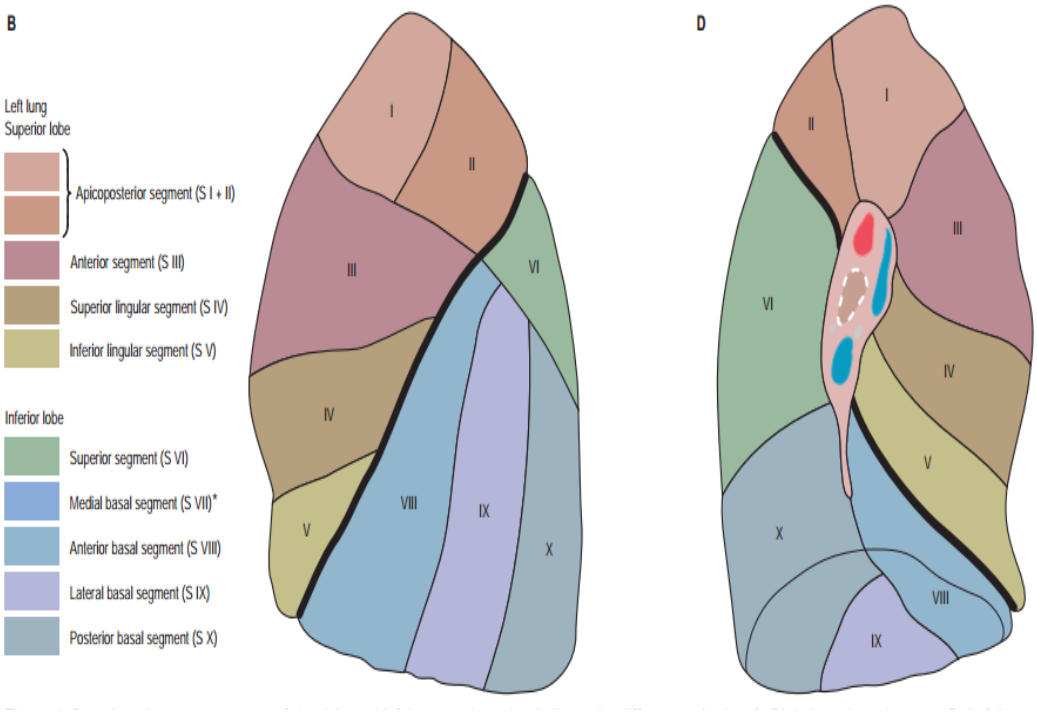


Figure 1.7 Bronchopulmonary segments of Left Lungs

(Netter, 2010)

1.5 BLOOD SUPPLY OF LUNGS

The lungs are supplied with deoxygenated blood by the paired pulmonary arteries. Once the blood has received oxygenation, it leaves the lungs via four pulmonary veins (two for each lung). The bronchi, lung roots, visceral pleura and supporting lung tissues require an extra nutritive blood supply. This is delivered by the bronchial arteries, which arise from the descending thoracic aorta. The bronchial veins provide venous drainage. The right bronchial vein drains into the azygos vein, whilst the left drains into the accessory hemiazygos vein (Moore et al., 2018) (Figure 1.5)

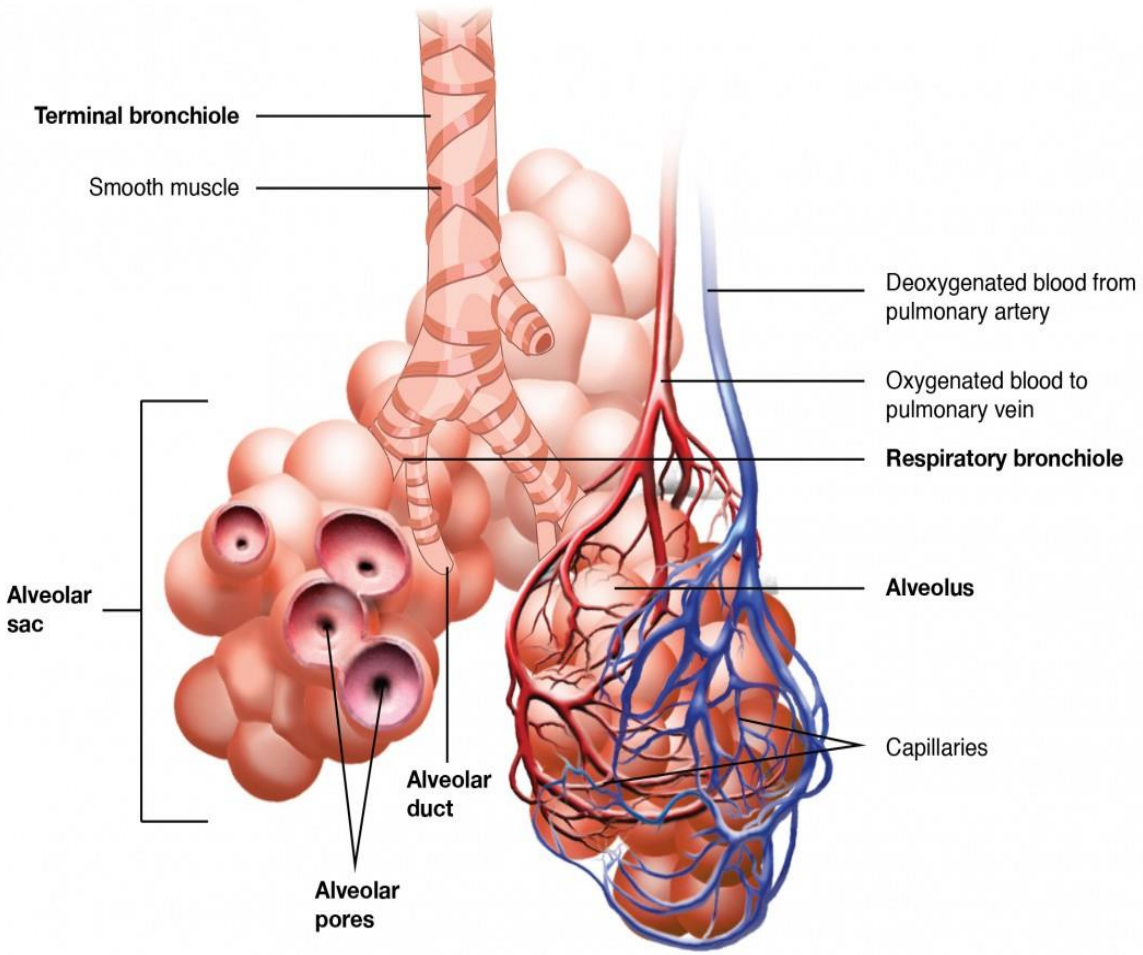


Figure 1.8 Blood supply of lungs

(Netter, 2010)

1.6 HISTOLOGY OF LUNG

The respiratory system consists of lungs and numerous air passages, of various sizes that lead to and from each lung. In addition, the system consists of a conducting portion and a respiratory portion. The conducting portion of the respiratory system consists of passageways outside (extra pulmonary) and inside (intrapulmonary) the lungs that conduct air for gaseous exchange to and from the lungs. In contrast, the respiratory portion consists of passageways within the lungs that not only conduct the air, but also allow for respiration, or gaseous exchange. The extra pulmonary passages, which include the trachea and primary bronchi, are lined by a pseudostratified columnar ciliated epithelium containing numerous goblet cells. As the passageways enter the lungs, the bronchi undergo extensive branching and their diameters become progressively smaller. There is also a gradual decrease in the height of the lining epithelium, amount of cilia, and number of goblet cells in these tubules. The bronchioles represent the terminal portion of the conducting passageways. These give rise to the respiratory bronchioles, which represent the transition zone between conducting and respiratory portions. The respiratory portion consists of respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli. Gaseous exchange in the lungs takes place in the alveoli, the terminal air spaces of the respiratory system. In the alveoli, goblet cells are absent and the lining epithelium is thin simple squamous. (Eroschenko& Di Fiore, 2013)

Conducting Portion of Respiratory System

The conducting portion of the respiratory system consists of the nasal cavities, pharynx, larynx, trachea, extra pulmonary bronchi, and a series of intrapulmonary bronchi and bronchioles with decreasing diameters that end as terminal bronchioles. Hyaline cartilage provides structural support and ensures that the larger air passageways are always patent (open). Incomplete C shaped hyaline cartilage rings encircle the trachea. Elastic and smooth muscle fibers, called the trachealis muscle, bridge the space between the ends of the hyaline cartilage. The cartilage rings of the trachea face posteriorly and are located adjacent to the esophagus. As the trachea divides into

primary bronchi which enter the lungs, the hyaline cartilage rings are replaced by irregular hyaline cartilage plates that encircle the bronchi. As the bronchi continue to divide and decrease in size, the cartilage plates also decrease in size and number. When the diameter of bronchioles decreases to about 1 mm, cartilage plates completely disappear from conducting passageways. Terminal bronchioles represent the final conducting passageways and have diameters ranging from 0.5 mm to 1.0 mm. There are between 20 and 25 generations of branching before the passageways reach the size of terminal bronchioles. The larger bronchioles are lined by tall, ciliated pseudostratified columnar epithelium that is similar to that of the trachea and bronchi. As the tubular size decreases, the epithelial height is gradually reduced, and the epithelium becomes simple ciliated cuboidal. The epithelium of larger bronchioles also contains numerous goblet cells. The number of these cells gradually decreases with the decreasing tubular size, and the goblet cells are not present in the epithelium of terminal bronchioles. Smaller bronchioles are lined only by simple cuboidal epithelium. In place of the goblet cells, another type of cells, called Clara cells, is found with the ciliated cells in the terminal and respiratory bronchioles. Clara cells are nonciliated, secretory cuboidal cells that increase in number as the number of ciliated cells decreases. (Mescher, 2021)

Respiratory Portion of the Respiratory System

The respiratory portion of the respiratory system is the distal continuation of the conducting portion and starts with the air passageways where respiration or gaseous exchange occurs. Terminal bronchioles give rise to respiratory bronchioles, which exhibit thin-walled out pocketing’s called alveoli and where respiration can take place. The respiratory bronchioles represent the transitional zone between air conduction and gaseous exchange or respiration. Respiration can only occur in alveoli because the barrier between inspired air in the alveoli and venous blood in capillaries is extremely thin. Other intrapulmonary structures in which respiration occurs are the alveolar ducts and alveolar sacs. In addition to the cells in the passageways, there are other cell types in the lung. The alveoli contain two cell types. The most abundant cells are the squamous alveolar cells or type I pneumocytes. These are extremely thin flat cells that line all alveolar surfaces. Interspersed among the squamous alveolar cells either singly

or in small groups are the type II pneumocytes. Lung macrophages, derived from circulating blood monocytes, are also found both in the connective tissue of alveolar walls or interalveolar septa (alveolar macrophages) and in the alveoli (dust cells). Also present in the interalveolar septa are extensive capillary networks, pulmonary arteries, pulmonary veins, lymphatic ducts, and nerves. (Ross &Pawlina, 2006)

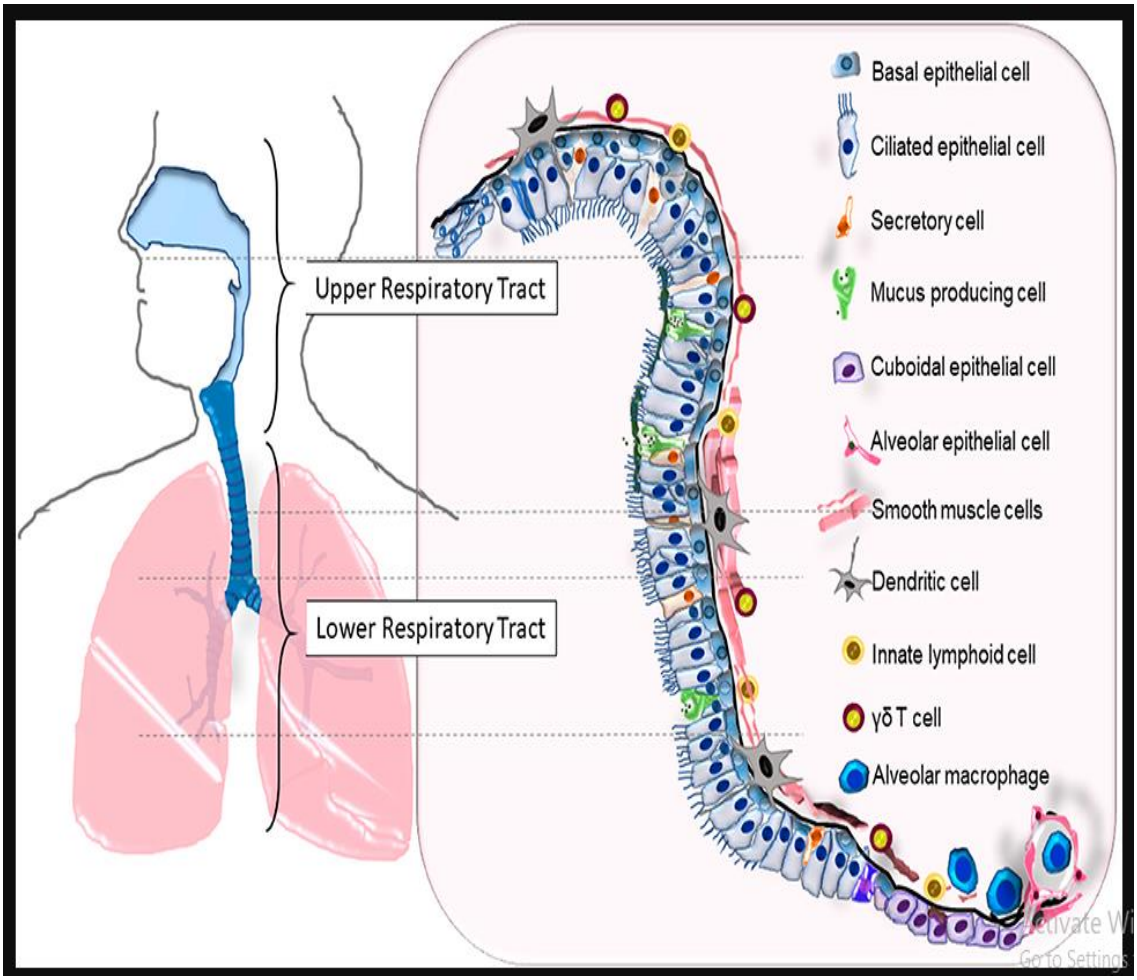


Figure 1.9 Cells present at different parts of lungs
(lungs.thecommonvein.net/histology)

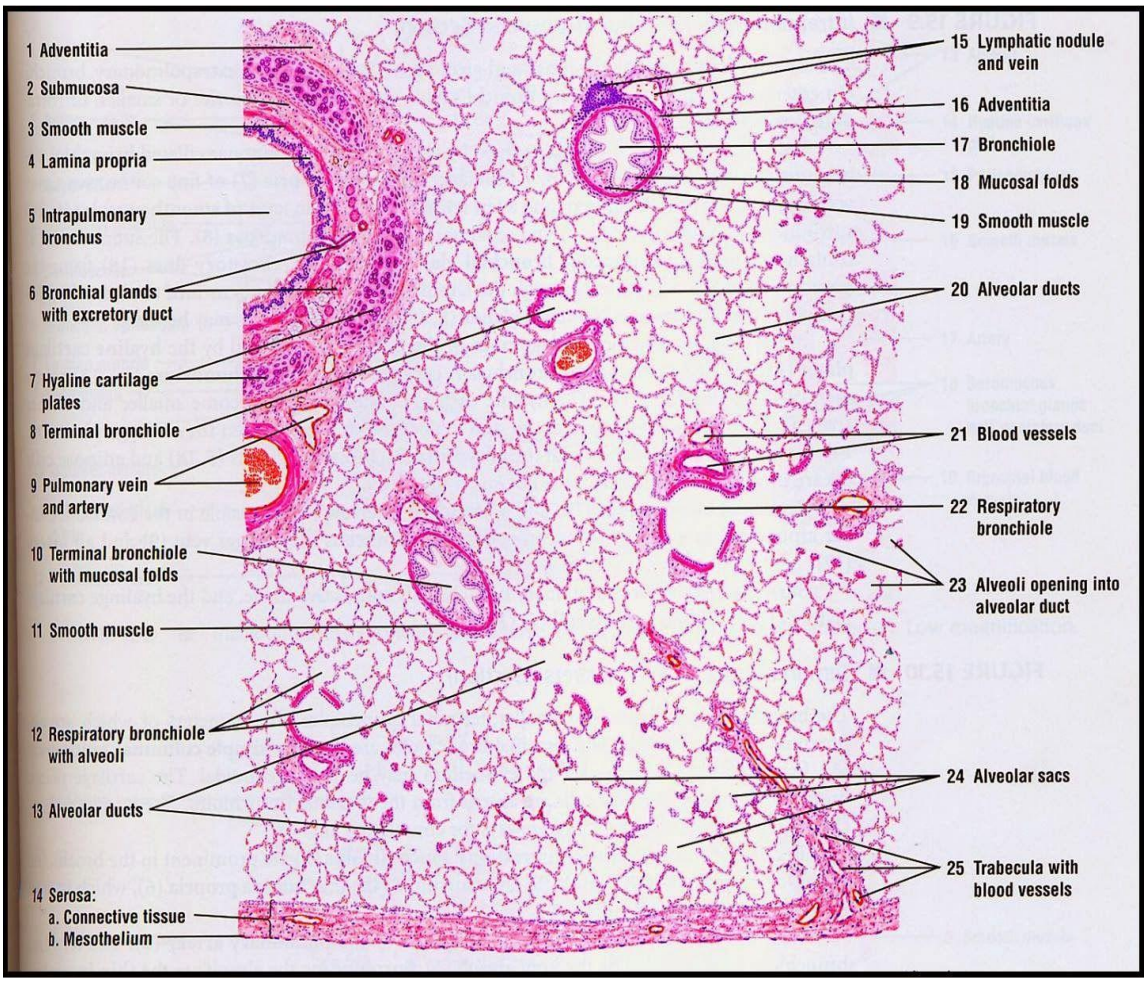


Figure 1.10 Histology of lung
(Mescher, 2016)

1.7 PLEURA

The visceral and parietal pleura are smooth serous membranes continuous with each other at the lung hila. The pleural space is a cavity between the 2 pleurae into which the lung protrudes. The visceral pleura is the one that covers both the lungs. The parietal and visceral pleurae are separated by a thin layer of fluid. This fluid contains molecules secreted by the mesothelial cells of the pleura which have surfactant like properties. (Moore et al., 2020)

1.8 EMBROLOGY OF RESPIRATORY TRACT

1.8.1 TRACHEA

The trachea starts to develop as a ventral outgrowth from the endodermal foregut into the mesenchyme that surrounds the sinus venosus and inflow tract of the heart. The point at which the original respiratory diverticulum buds form from the foregut, the laryngo tracheal groove, remains at a constant level during the embryonic period, and the trachea lengthens distally as the bifurcation point descends. Initially, the tracheal mesenchyme is continuous with that surrounding the ventral wall of the esophagus. Progressive lengthening and continued division of the tracheal bud, together with deviation of the lung buds dorsally, isolates the esophagus and trachea within tissue specific mesenchyme and facilitates regional differentiation, not only between trachea and lungs, but also within the lungs themselves, i.e. the number of lobes, or the degree of growth and maturity of a particular lung. (Figure 1.11)(Moore, Persaud and Torchia 2018)

Each lung develops by a process of dichotomous branching. For branching to occur, a cleft must develop in the tip of the epithelial tube. The epithelium then evaginates each side of the cleft, forming new branches that lengthen, and the process is then repeated. In the normal neonate, the trachea is relatively small in relation to the larynx. The walls of the trachea are relatively thick and the tracheal cartilages are

relatively closer together than in the adult. The trachea begins at the upper border of the sixth cervical vertebra, a relationship that is conserved with growth, and it bifurcates at the level of the third or fourth thoracic vertebra. (Figure 1.11)(Sadler, 2018)

1.8.2 LUNGS

During intrauterine life, the developing fetus is not only dependent on the expectant mother for nourishment, but also to get rid of its waste matter. Even though the fetal lungs does not participating in gas exchange throughout the pregnancy, its development is necessary to support the fetus. There are three fundamental features that the lungs must develop in order to facilitate the transition from placental gas exchange to pulmonary gas exchange. The lungs must first increase the amount of surfactant. This is mixture of phospholipids and protein which helps to reduce the surface tension in the alveoli and allows them to expand with inhalation. Secondly, the lungs must acquire a gas exchange capacity. This occurs once the alveolar units begin to develop in late pregnancy. Thirdly, there needs to be a parallel dual circulation that allows blood to be oxygenated, and the lung parenchyma to be perfused. Lung maturation ensues throughout the embryonic period and continues into childhood (up to the age of 8). Embryonic lung maturation occurs in four stages that are regulated by intricately arranged biochemical cascades. These stages are known as the pseudoglandular, canalicular, terminal sac, and alveolar stages. The development of the lung parenchyma occurs in relation to the development of the bronchopulmonary tree. By the 5th gestational week, the splanchnic mesenchyme that surrounds the bronchial buds (terminal branches of the laryngo tracheal diverticulum) begins to expand. The splanchnic mesenchyme also releases many signaling proteins (including fibroblast growth factor 10), which promotes the growth of the respiratory buds. Therefore the growth of the splanchnic mesenchyme occurs concurrently with the expansion and ramification of the bronchial buds. While the bronchial buds give rise to the bronchi and bronchioles, the splanchnic mesenchyme forms the lung parenchyma**.** (Figure 1.12)(Moore et al., 2018)

By the 6th gestational week, lung development enters the pseudoglandular stage. Histologically, the tissue is arranged in a tubuloacinar pattern; much like that observed in exocrine glands. These features are dominant throughout the early stage of pregnancy, up to the 16th gestational week. At this stage, the maturing lung contains the conductive entities of the lung. However, the gas exchange components are not yet formed. Therefore, if a baby born at this gestational age, the infant is unlikely to survive since structure involved in gaseous exchange are not formed. Within the lung, there is a disparity in the rate of development of the lung such that the lung apices mature faster than the lung bases. Consequently, while the lung bases may still be in the pseudoglandular phase, the apices would have transitioned into the canalicular phase. This period, which lasts from the 16th to the 26th gestational week, is characterized by the formation of the primordial alveolar ducts. The formation of these tubules is preceded by dilation of the bronchial lumen and terminal bronchioles as well. Around the 24th gestational week, the terminal bronchioles divide to give at least two respiratory bronchioles. Each respiratory bronchiole subsequently separates to give up to six primordial alveolar ducts. There are terminal sacculations at the end of the primordial alveolar ducts known as primordial alveoli. The walls of these sacs are thin enough to facilitate gas exchange where the lungs acquire significant vascular tree at this point. Therefore, an infant born within this period has a chance at surviving. However, they are likely to face other challenges with other poorly developed organ systems. Towards the end of the 26th gestational week, more primordial alveoli, with thinner walls develop. In this terminal sac phase of lung development, the walls of the sacs are lined by endoderm-derived squamous epithelium. These cells are referred to as type I pneumocytes and these cells involved in gaseous exchange. Dispersed among them are type II pneumocytes. These cells are round secretory cells that produce surfactant. Even though the lungs began producing and secreting surfactant as early as 20 to 22 weeks, the quantity significantly increases during the last two weeks of pregnancy. The terminal sac phase continues from the 26th gestational week through to delivery of the infant. Although there is an increase in the amount of surfactant being produced, it isn't sufficient to efficiently support life prior to the 32nd gestational week. Therefore, infants born prior to 32 weeks have a fighting chance of surviving with medical intervention.(Standring,2020)

The final maturation of the primordial alveoli begins from the 32nd gestational week and continues up to the 8th year of life. The stage begins with clusters of alveolar sacs at the end of the respiratory bronchioles. The sacs subsequently differentiate into alveolar ducts. Additionally, the vascular beds can be seen bulging into the alveolar wallsas the sacs become progressively thinner. Eventually, the walls of the capillary beds and the type I pneumocytes become so closely related that they form the alveolocapillary membrane. This interface is the also known as the respiratory membrane or the pulmonary diffusion barrier. As the name suggests, it acts as the point of gas exchange between the alveoli and the surrounding capillaries. At this stage, the lungs are capable of supporting life; therefore, an infant born at this point and beyond is more likely to survive. Even though these significant events occur in utero, the majority of alveolar maturation occurs during extra uterine life. There is a significant increase in the number of primordial alveoli and respiratory bronchioles, as well as distension of the primordial alveoli after birth. Overall, both factors account for the increase in the size of the lungs; although the increase in the quantity of the respiratory entities plays a bigger role than does expansion of the primordial alveoli. There are other events that occur within the uterus that promotes lung maturation. The fetal breathing movements and the amount of amniotic fluid present in the amniotic sac both influence the fetal lung development. A fetal breathing movement occurs before births that result in aspiration of some amniotic fluid into the lungs. They occur occasionally but become more frequent during last month of the gestation. (Moore et al.2018).

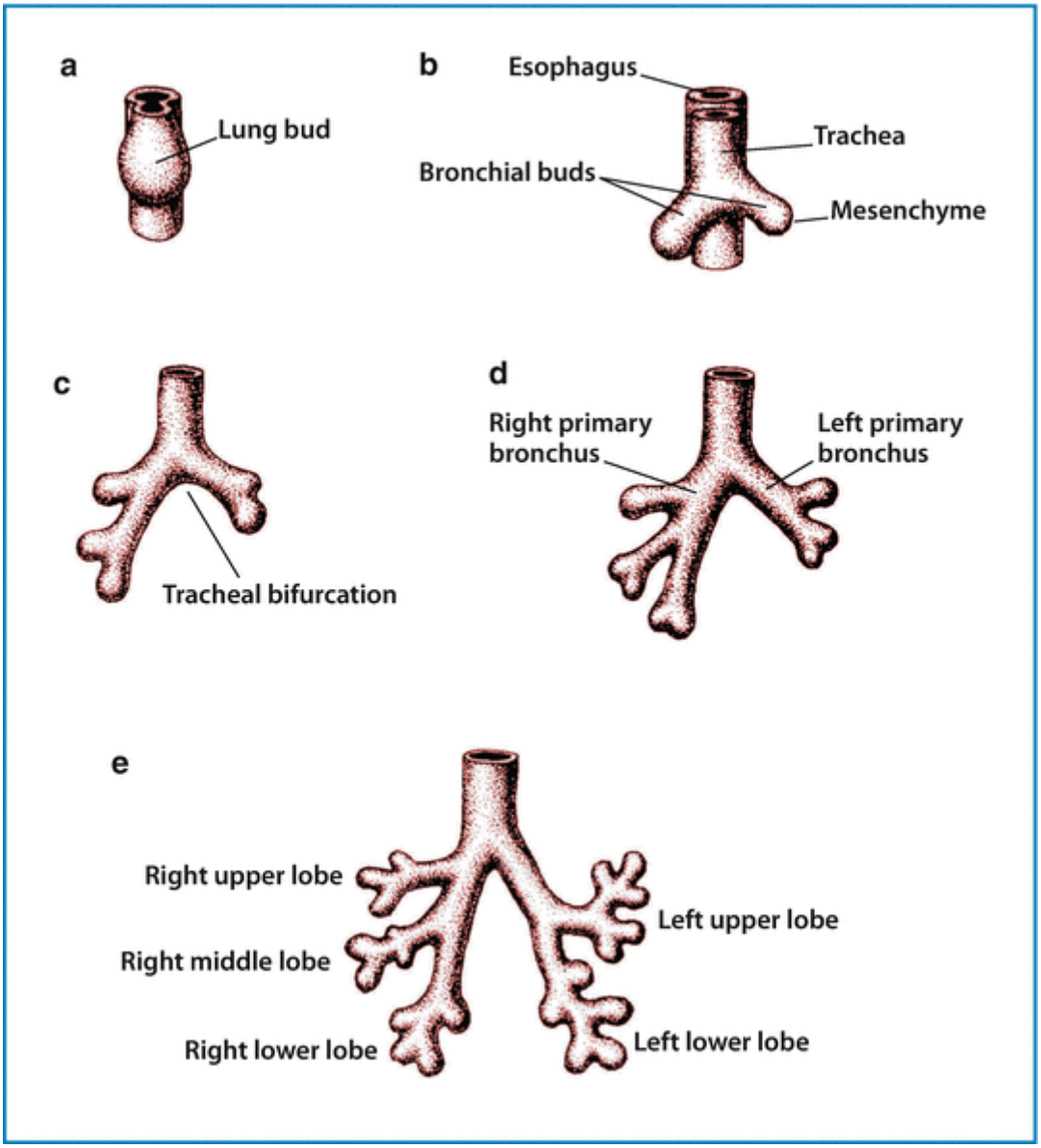


Figure 1.11 Development of respiratory tree and diaphragm

(springer.com)

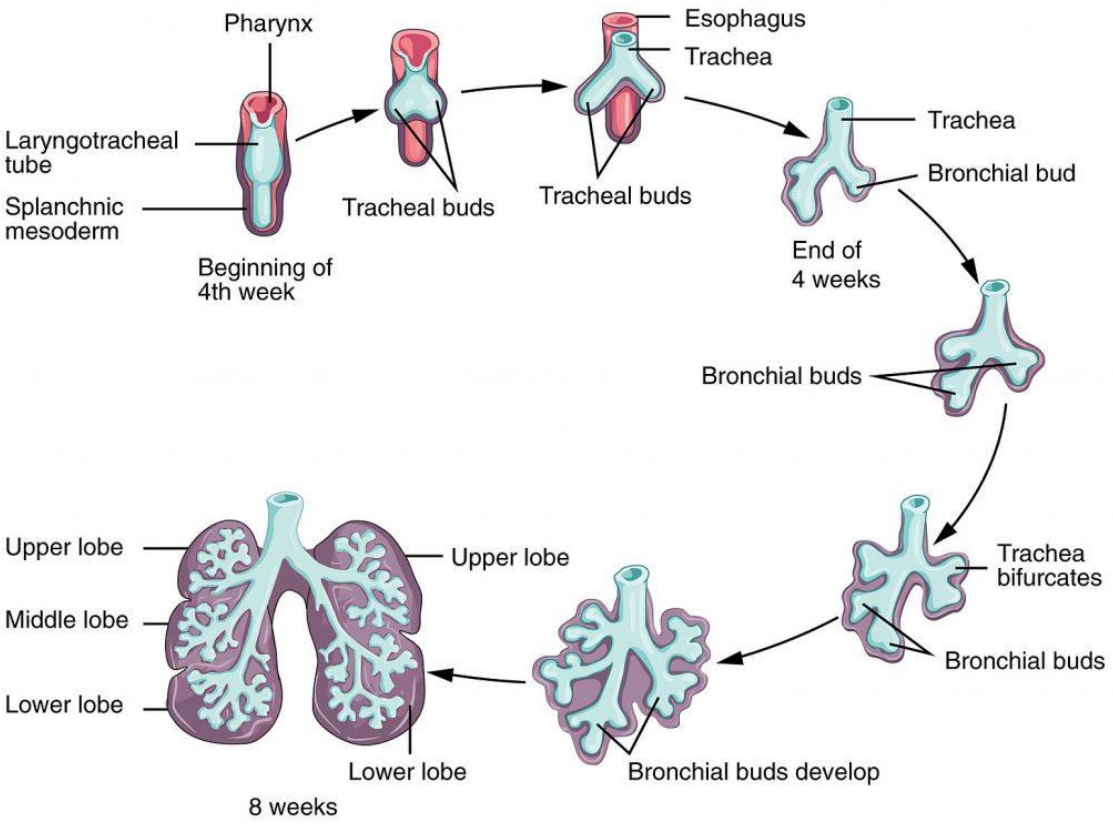


Figure 1.12 Developmental stages of lungs
(teachmeanatomy.com)

1.9 ANATOMY OF HEART

The heart is muscular organs which collects deoxygenated blood from the body, carries it to the lungs for oxygenation and removes carbon dioxide. Then, the oxygenated blood is transported from the lungs for distribution to all parts of the body. The heart consist of four chambers: the left atrium and right atrium are two upper chambers and the left and right ventricles are two lower chambers. There are four valves in the heart to control the flow of blood: the tricuspid, pulmonary, mitral and aortic valves. The non-oxygenated blood enters the right atrium from the largest veins of the body superior vena cava which receives the deoxygenated blood from upper half of the body and inferior vena cava which receives blood from lower half of body and pumps it through the tricuspid valve to the right ventricle. From the right ventricle deoxygenated blood pumps through the pulmonary valve and pulmonary artery to the lungs and becomes oxygenated. The oxygenated blood enters the left atrium from the lungs and pumps it through the mitral valve to the left ventricle. From the left ventricle oxygen rich blood pumps through the aortic valve to the aorta and the whole body. The heart muscles are supplied by coronary arteries which run along the surface of the heart. The nerve tissue also runs through the heart wall, conducting the complex signals that govern contraction and relaxation. The pericardium surrounds the heart and roots of the major blood vessels, the outer layer known as parietal pericardium and inner layer known as visceral pericardium. (Moore et al., 2020)

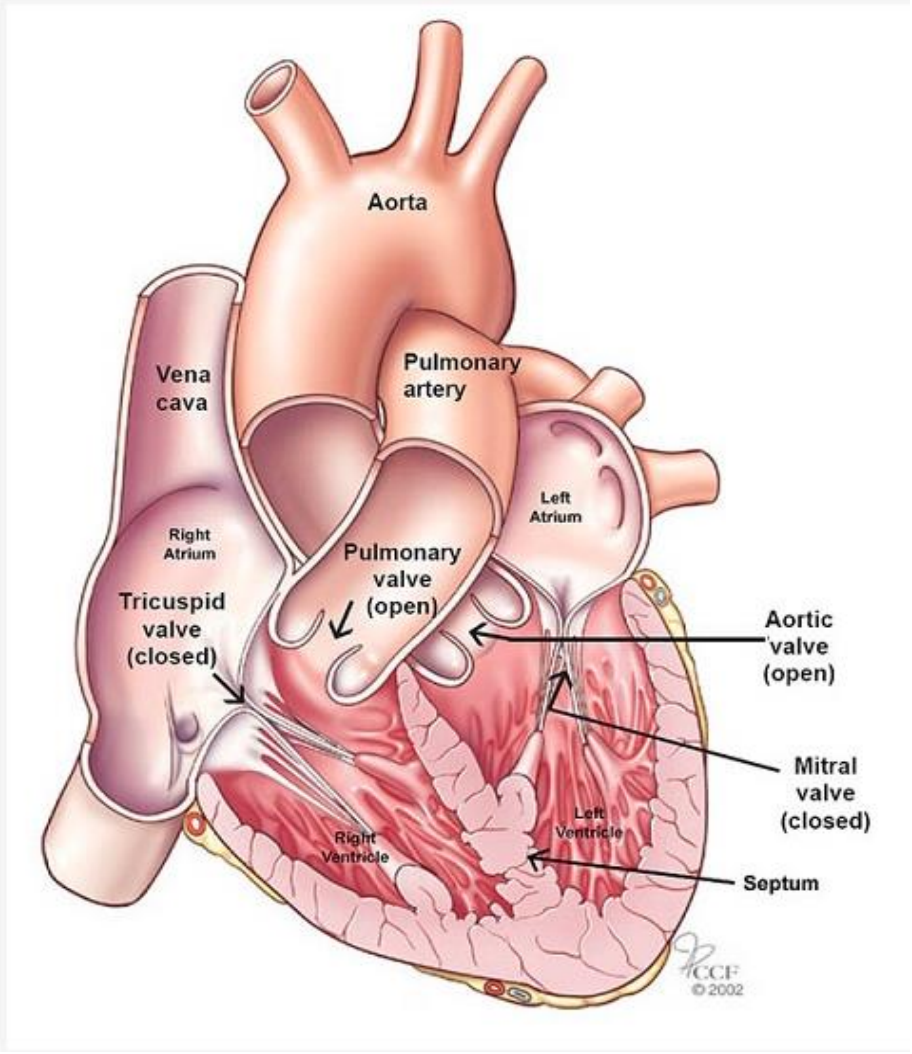


Figure 1.13 Anatomy of heart
(Clevelandclinic.org)

1.10 DEVELOPMENT OF THE HEART

Development of the heart begins in the third week with the formation of two endothelial strands called the angioblastic cords. These cords canalize forming two heart tubes, which fuse into single heart tube by the end of the third week due to lateral embryonic folding. By the fourth week, the developing heart receives blood from three pairs of veins: the vitelline veins, umbilical veins, and common cardinal veins into the sinus venosus. The vitelline veins carry poorly oxygenated blood from the yolk sac, and enter the sinus venosus; the umbilical veins carry oxygenated blood from the chorion, the primordial placenta; and the common cardinal veins carry poorly oxygenated blood from the rest of the embryo. As the primordial liver develops in close association with the septum transversum, the hepatic cords join and surround epithelial-lined spaces, forming the primordial hepatic sinusoids. These primordial sinusoids become connected to the vitelline veins. Vitelline veins pass through the septum transversum and enter sinus venosus, also called as venous end of the heart. Left vitelline veins regress while right vitelline veins form the hepatic veins, and a network of vitelline veins around the duodenum form the portal vein. As the development of liver progresses, umbilical veins lose connection with heart and empty into liver. The right umbilical vein and cranial part of the left umbilical vein degenerate during seventh week of gestation, leaving only the caudal part of the left umbilical vein. The caudal part of the left umbilical vein carries oxygenated blood to the embryo from the placenta. The umbilical vein is connected to the inferior vena cava (IVC) via the ductusvenosus, a venous shunt that develops in the liver. The blood directly passes to the heart from placenta without passing through liver. (Moore et al., 2018)

1.11HEART LAYERS

As the heart tubes fuse, the primordial myocardium begins to form from the splanchnic mesoderm around the pericardial cavity. This primordial myocardium becomes the middle, muscular layer of the heart. Separated from the primordial myocardium by gelatinous tissue called cardiac jelly, the heart begins to develop as a thin tube. This endothelial tube becomes the endocardium, the innermost layer of the

heart. Epicardium, the outermost layer, originates from mesothelium cells from the outer surface of the sinus venosus. (Moore et al., 2018)

1.12HEART TUBE

As the cranial part of the embryo folds, the heart tube elongates. As it elongates, the heart tube develops alternating constrictions and expansions, forming the bulbuscordis, ventricle, atrium, and sinus venosus. The bulbuscordis has three components, including the truncusarteriosus, conusarteriosus, and conuscordis. The truncusarteriosus is caudal to the aortic sac, to which it is connected, and gives off the pharyngeal arch arteries. Blood leaves the heart via the pharyngeal arch arteries, and returns to the sinus venosus of the heart via the umbilical, vitelline, and common cardinal veins. The bulbuscordis and ventricles grow at a faster rate than other parts of the developing heart, and because of this the heart bends and folds in on itself, forming the bulbo-ventricular loop. As this bending occurs, the atrium and sinus venosus move so that they are dorsal to the truncusarteriosus, bulbuscordis, and ventricle. During this time, the sinus venosus also develops lateral extensions, the left and right horns. The heart is initially attached to the dorsal wall of the pericardial cavity by a mesentery called the dorsal mesocardium, but as the heart grows it begins to fill the pericardial cavity and the central part of the dorsal mesocardium degenerates. (Moore et al., 2018)

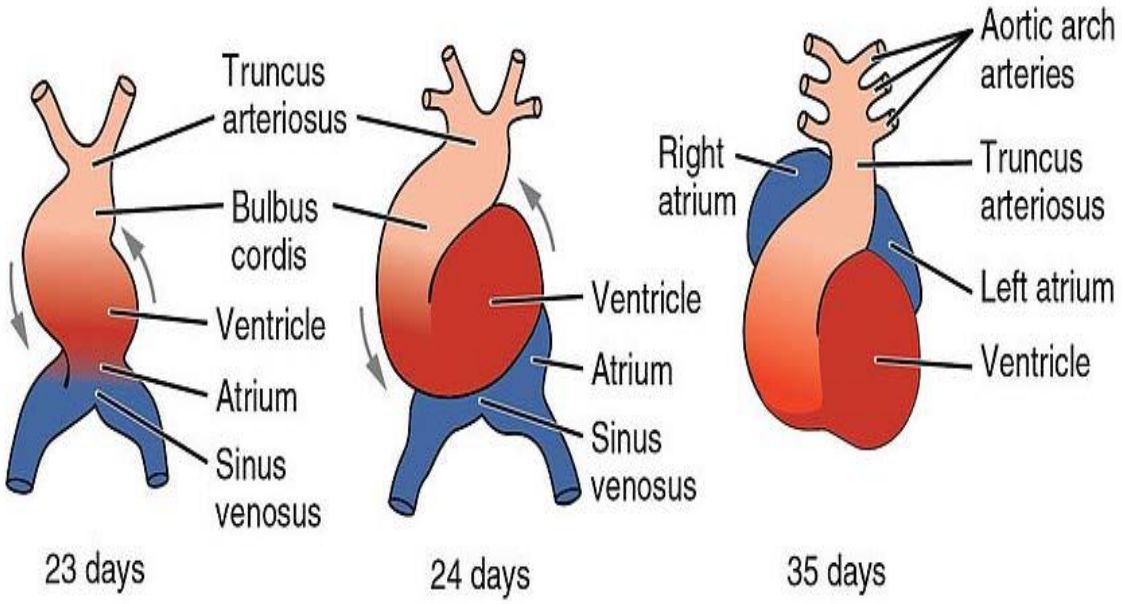


Figure 1.14 Process of heart tube looping

1.13PARTITIONING OF THE DEVELOPING HEART

In the middle of the fourth week, the atrioventricular canal, primordial atrium and ventricle start to partition, and this process is completed by the end of week eight. It begins with the formation of the endocardial cushions, specialized neural crest derivatives extracellular matrix tissue related to myocardial tissue. At the end of the fourth week, these cushions appear on the ventral and dorsal walls of the AV canal and start to grow toward each other. The primordial atrium becomes separated into the right and left atria by two septa, the septum primum and septum secundum. The septum primum appears first in the form of a thin membrane, growing out of the roof of the primordial atrium toward the endocardial cushions, leaving an opening between its edge and endocardial cushion. This opening is called the foramen primum, and it allows blood to be shunted from the right atrium to the left. It progressively shrinks and eventually closes as the septum primum elongates and fuses with the endocardial cushions, forming the primordial AV septum. Before the foramen primum closes completely, apoptosis of cells in the middle of the septum primum forms perforations in the septum. These perforations form a new second opening, the foramen secundum, which allows oxygenated blood to continue to flow from the right atrium to the left. The muscular septum, the septum secundum, grows immediately adjacent to the septum primum, just to its right. It grows downward from the ventral and cranial wall of the atrium during the fifth and sixth weeks of development, gradually overlapping the foramen secundum in the septum primum. By overlapping the foramen secundum without fusing to the septum primum, an incomplete barrier between the atria is formed. This opening between the atria is called the foramen ovale, and it allows oxygenated blood to continue to flow from the right atrium, under the flap of the septum secundum, through the foramen secundum, and into the left atrium. This arrangement prevents blood from flowing in the opposite direction. The cranial part of the septum primum slowly regresses, lower parts of the septum primum remain attached to the endocardial cushions and forms the valve of the foramen ovale. (Standring, 2020)

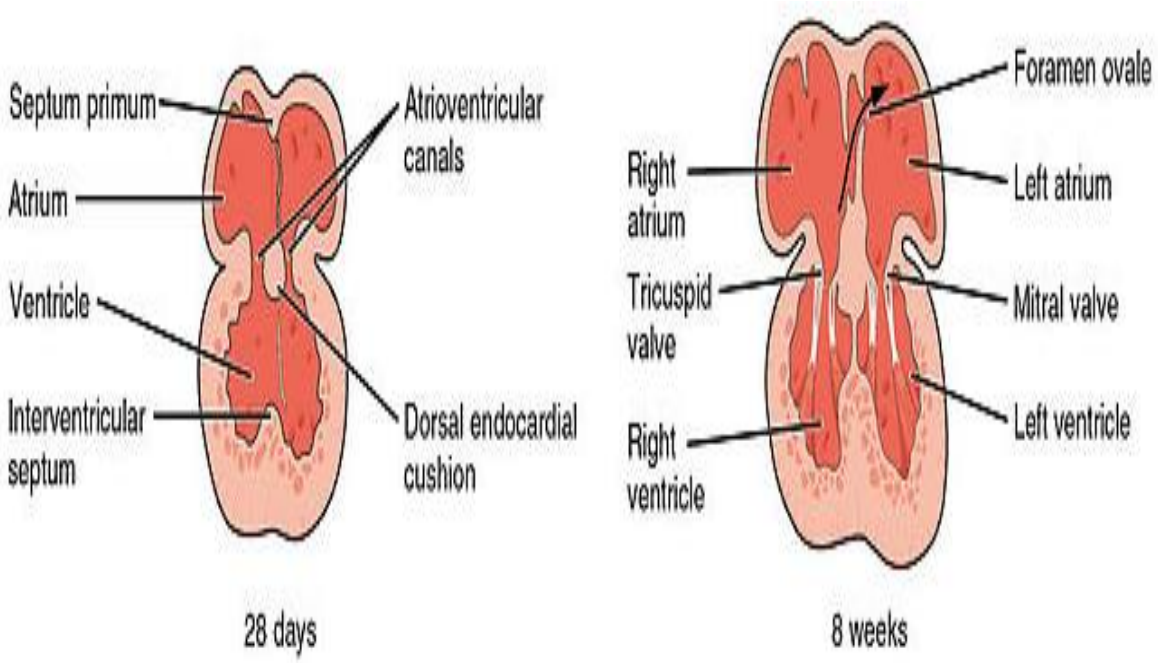


Figure 1.15 Separation of atria and ventricles
(teachmeanatomy.info)

1.14 CT SCAN

Computed tomography is commonly referred to as a CT scan. A CT scan is a diagnostic imaging procedure that uses a combination of X-rays and computer technology to produce images of the inside of the body. It shows detailed images of any part of the body, including the bones, muscles, fat, organs and blood vessels. (Hopkins medicine .org)

High-Resolution Computed Tomography (HRCT)

HRCT is computed tomography (CT) with high resolution. It is used in the diagnosis of various health problems. HRCT involves the use of special computed tomography scanning techniques to assess the lung parenchyma which enables it to diagnose certain lung diseases better than conventional radiography. (Lauri, 2017)

1.15 CT SCAN FINDINGS OF COVID 19

The ground-glass opacity (GGO) are the most frequent and earliest pattern that appear on CT scan which may be unifocal, multifocal, bilateral, and peripheral distribution with a posterior predominant posteriorly and inferiorly. Common findings are the traction bronchiectasis and widening of vessels in the area of GGO (Kanne et al., 2020; Kovasc et al., 2020)

Interlobular and interlobular lines appear thickened in the GGO. This is known as crazy paving pattern. It is only the feature of COVID 19 pneumonia and not characteristic for other viral pneumonias. The differential diagnosis can be made on this characteristic (Pan et al., 2020; Kovasc et al., 2020)

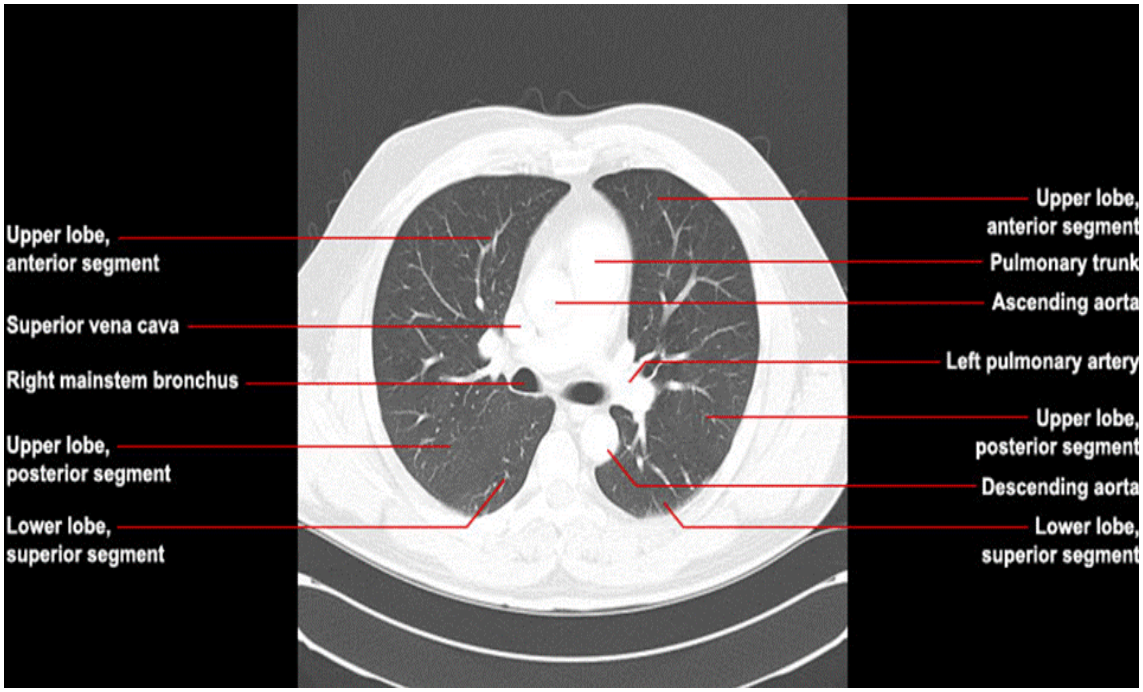


Figure1.16 Chest CT image
(radiologyinfo.org)

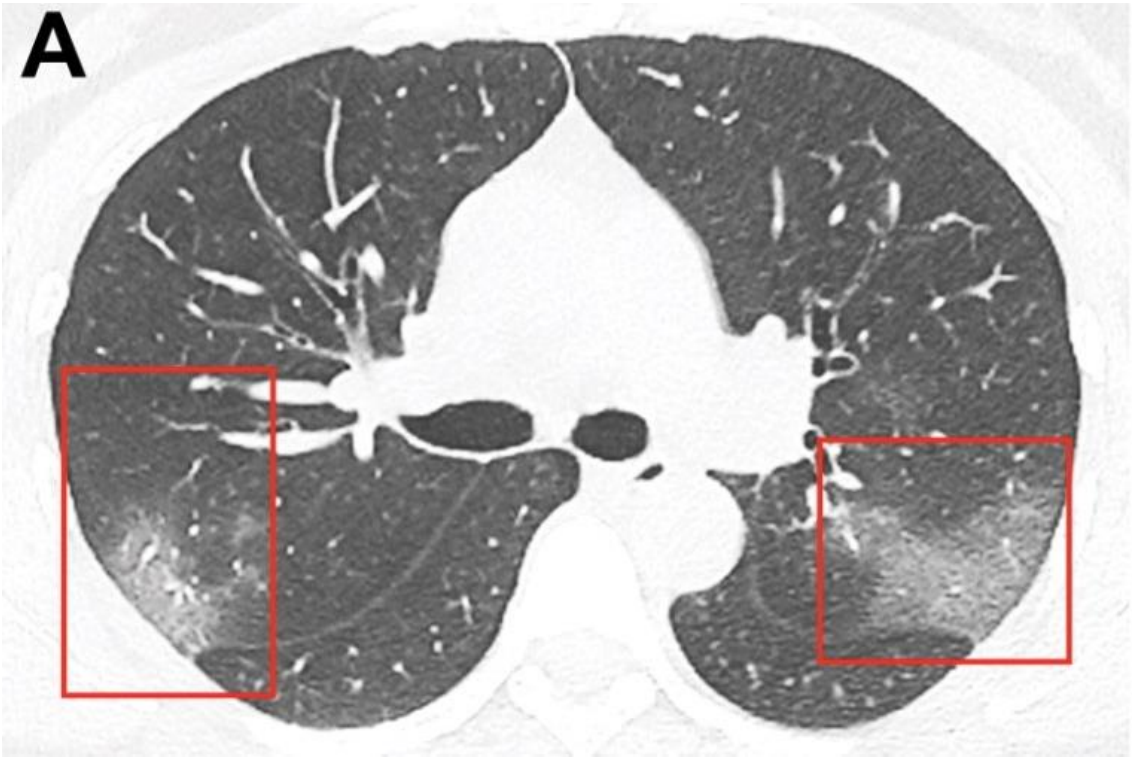


Figure 1.17 CT scan shows fibrosis of lungs
(radiologyinfo.org)

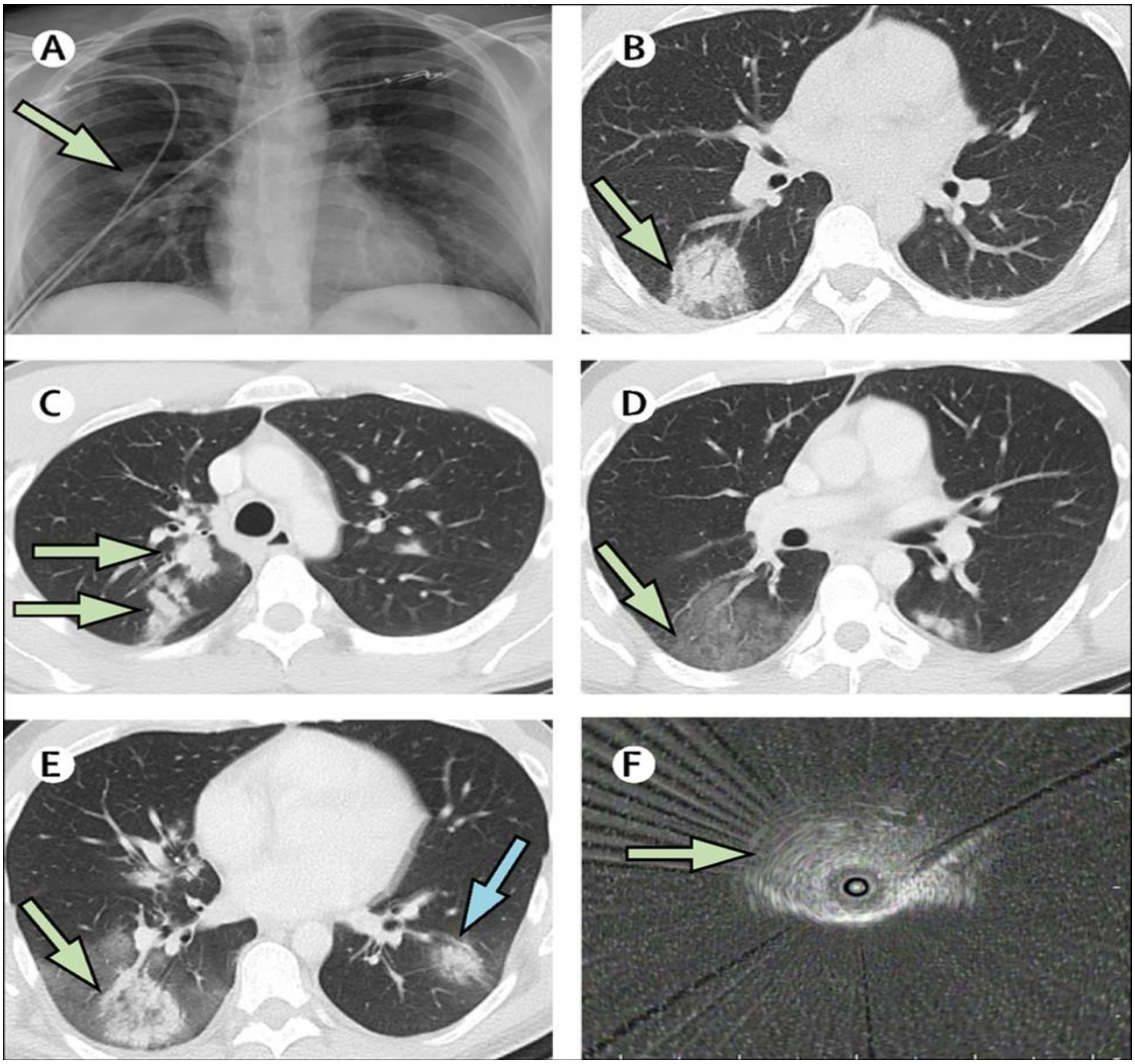


Figure 1.18 HRCT scan chest (radiologyinfo.org)

A: Green arrow pointing towards GGO of lungs

B: Green arrow pointing towards consolidation of lungs

C: Green arrow pointing towards consolidation of lungs

D: Green arrow Arrow pointing towards GGO of lungs

E: Green arrow pointing towards consolidation of lungs Blue arrow pointing towards GGO of lungs

F: Green arrow pointing towards honeycomb appearance

Radiology plays a significant role in the diagnosis and management of COVID-19 pneumonia. The first-line imaging modality is to be considered as CT scan in highly suspected cases and is also helpful in monitoring the changes in lungs during infection and recovery period. Therefore, it is identified as efficient clinical diagnostic tool for people with suspected COVID-19. CT scan has potential for identifying disease in negative results of a reverse transcription–polymerase chain reaction (RT-PCR) assay COVID-19 is highly suspected due to symptoms. The most common clinical presentation of COVID-19 is Pneumonia which involves both lungs simultaneously. The severity of disease can be reflected by findings on CT scan. The detailed imaging features and differences in imaging features between the four clinical types (mild, common, severe, fatal) have not been well studied for this disease. (Qin et al; 2020)

The detected lung abnormalities in patients with COVID-19 such as GGO, crazy pacing pattern and consolidation peak around 6-11 days after the onset of the disease. The CT scan findings may improve around 14 days; the absorption stage may extend beyond 26 days. (Gianella et al., 2020)

Long term effect of COVID 19 on lungs and heart can be detected on CT scan. Some studies state that 6 month follow up CT scan of COVID 19 survivors shows permanent fibrotic changes in lungs. Fibrosis can shrinks the size of lung and which will ultimately affect the pulmonary function test on Spirometry. Patient may complain of dyspnea even after 6 month of recovery from disease. It is necessary to investigate the long term effects of COVID 19 disease on lungs and heart. (Zhao et al; 2020)

Typical and atypical imaging findings of COVID-19 infection have been extensively reported. A meta-analysis including twenty-eight studies and 3,466 patients has been recently published to optimize the diagnostic interpretation of chest CT scanning for COVID-19. In patients without severe respiratory disease, the major pulmonary CT findings of COVID-19 are ground-glass opacities (GGOs) with a typical bilateral and multilobar distribution and middle-lower lung predominance, mainly with a subpleural distribution. In more severely affected patients, consolidation replaces GGO, and the abnormalities extend to the upper lobes or become bilateral. (Liu et al., 2020)

However, little is known about sequential CT scan findings during the subsequent course of COVID-19, especially about sequelae that may occur during

convalescence. Expiratory CT has established itself as an essential adjunct to conventional CT, in the demonstration of air trapping in patients with suspected obstructive small airway disease. In our institution, paired inspiratory/expiratory CT examination is obtained routinely to evaluate patients in whom airway disease is suspected. (Franquet et al., 2020)

CT scans is the base line to diagnose fibrosis in the lung in patients recovered from moderate or severe COVID-19 pneumonia. (Ahmet et al., 2020) Multiple organs are damaged by COVID 19, but lungs are mostly infected and pneumonia is the most common manifestation of infection ranging from mild to moderate cases to severe respiratory failure. (Matsuo et al., 2020)

1.16 SIGNIFICANCE OF STUDY

We aim to investigate changes in the size of lungs and heart on follow up computed tomography (CT) scan in patients with coronavirus disease 2019 COVID-19. Patients was undergo chest CT scan, symptom assessment, and pulmonary function tests after discharge from the hospital. This was the first study in Pakistan to diagnose long term sequel of COVID 19. In this study, we measured the size of heart and lung of COVID 19 survivors the information regarding long term effects of COVID 19 which is helpful in planning management of COVID 19 pneumonia because fibrotic changes of lungs may have deranged pulmonary function test resulting in dyspnea related problems.

1.17STATEMENT OF THE PROBLEM

Studies revealed that at six-month follow-up COVID 19 patients were still complaining of dry cough and experienced slight exertional dyspnea. Patients with lung fibrotic changes more commonly experienced dry cough. Patients who underwent PFT presented with abnormal pulmonary function tests.

1.18 HYPOTHESIS

NULL HYPOTHESIS:

There are no changes in lung and heart size and there are no permanent fibrotic changes in lungs of COVID 19 survivors

ALTERNATE HYPOTHESIS:

There is a decrease in lung size and heart size and permanent fibrotic changes in lungs of COVID 19 survivors

1.19 OBJECTIVES OF STUDY:

- To assess pulmonary sequel and explore the risk factor for lung fibrotic changes at 3 month follow up on HRCT scan chest of survivors of sever COVID-19 pneumonia.
- To assess the difference in lung size on HRCT scan chest of survivors of COVID 19 pneumonia and healthy controls
- To assess the difference in heart size on HRCT scan chest of COVID 19 survivor and healthy controls

CHAPTER 2

LITERATURE REVIEW

Thin-section HRCT scan chest could provide semi-quantitative analysis of severity of pulmonary damage. This disease changed speedily at the early stage, then tended to be stable and lung changes like fibrosis and ground glass opacities remain for a long time. (Ding et al., 2020)

Six-month follow-up of COVID 19 patients with severe respiratory distress treated and discharged from hospital their HRCT scan chest showed fibrotic-like changes in the lung in more than one-third of patients. These changes were associated with an acute respiratory distress syndrome, longer hospital stays, noninvasive mechanical ventilation, and higher initial chest HRCT score. (Xiong et al., 2020)

The extent of lung abnormalities at HRCT scan chest peaked during illness days 6–11. The temporal changes of the diverse HRCT manifestations followed a specific pattern, (ground glass opacities, Consolidation) which might indicate the progression and recovery of the illness. (Wang et al., 2020)

Typical radiographic images of COVID-19 demonstrated clear destruction of the lung parenchyma, including interstitial inflammation and extensive consolidation, similar to the previously reported coronavirus infection. (Fang pan et al., 2020)

The pulmonary dysfunction of SARS-CoV-2 patients improved over time, but patients did not fully recover even after 6 months. After 6 months of recovery, abnormal pulmonary HRCT findings and pulmonary dysfunction were still observed in some COVID-19 patients and, especially, imaging abnormalities were observed more frequently in severe patients. These observations suggest that patients with COVID-19

may suffer from persistent lung injury after viral infection and, thus, should be subjected to long-term follow-up. (Qin et al., 2020)

Most patients with COVID-19 infection have a mild illness and do not develop pneumonia the chest radiograph may be normal in up to 63% of people with covid-19 pneumonia, particularly in the early stages (but there is uncertainty around this estimate, ranging from0% to 63%) Changes include ground glass (68.5%), coarse horizontal linear opacities(28.5%), and consolidation(35.4%).These are more likely to be peripheral and in the lower zones, but the whole lung can be involved Ground glass appearance is common in earlier presentations and may precede the appearance of consolidation Bilateral lung involvement is most common (72.9%) (Cleverly et al., 2020)

Patients with confirmed COVID-19 pneumonia have typical imaging features that can be helpful in early screening of highly suspected cases and in evaluation of the severity and extent of disease. Most patients with COVID-19 pneumonia have GGO or mixed GGO and consolidation (figure 2.1) and vascular enlargement in the lesion. Lesions are more likely to have peripheral distribution and bilateral involvement and be lower lung predominant and multifocal. HRCT involvement score can help in evaluation of the severity and extent of the disease. (Zhao et al., 2020)

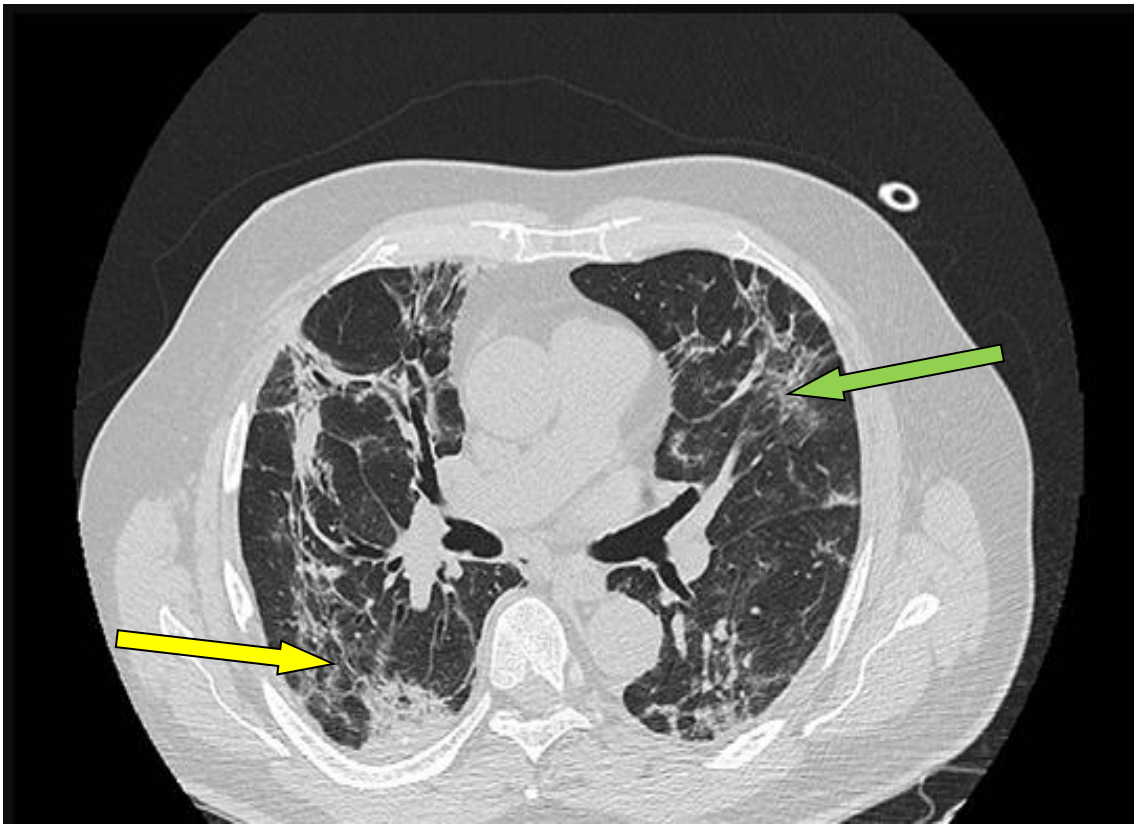


Figure 2.1 HRCT scan of COVID-19 patient. (radiologyinfo.org)
Yellow arrow: pointing towards peripheral vascular marking in lung
Green arrow: pointing towards GGO of lung

CT chest plays an important role in the diagnosis, staging, and monitoring of patients with COVID-19 pneumonia. In the early phase, multiple small patchy shadows and interstitial changes emerge, and show a distribution starting near the pleura or bronchi rather than pulmonary parenchyma.(Figure 2.2) In the progressive phase, the lesions increase and enlarge, developing into multiple GGOs as well as infiltrating consolidation in both lungs. In the severe phase, massive pulmonary consolidations and "white lungs" are seen, but pleural effusion is rare. In the dissipative phase, the GGOs and pulmonary consolidations were completely absorbed, and the lesions began to change into fibrosis (Li et al., 2020)

COVID-19 survivors were mainly troubled with fatigue or muscle weakness, sleep difficulties, and anxiety or depression. Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations, and are the main target population for intervention of long-term recovery (Huang et al., 2021)

Compared with the ordinary patients, the severe/critical patients had older ages, higher incidence of comorbidities, cough, expectoration, chest pain, and dyspnea. The incidences of consolidation, linear opacities, crazy-paving pat-tern, and bronchial wall thickening in severe/critical patients were significantly higher than those of the ordinary patients. Besides, severe/critical patients showed higher incidences of lymph node enlargement, pericardial effusion, and pleural effusion than the ordinary patients. The CT scores of severe/critical patients were significantly higher than those of the ordinary patients (Li et al., 2020)

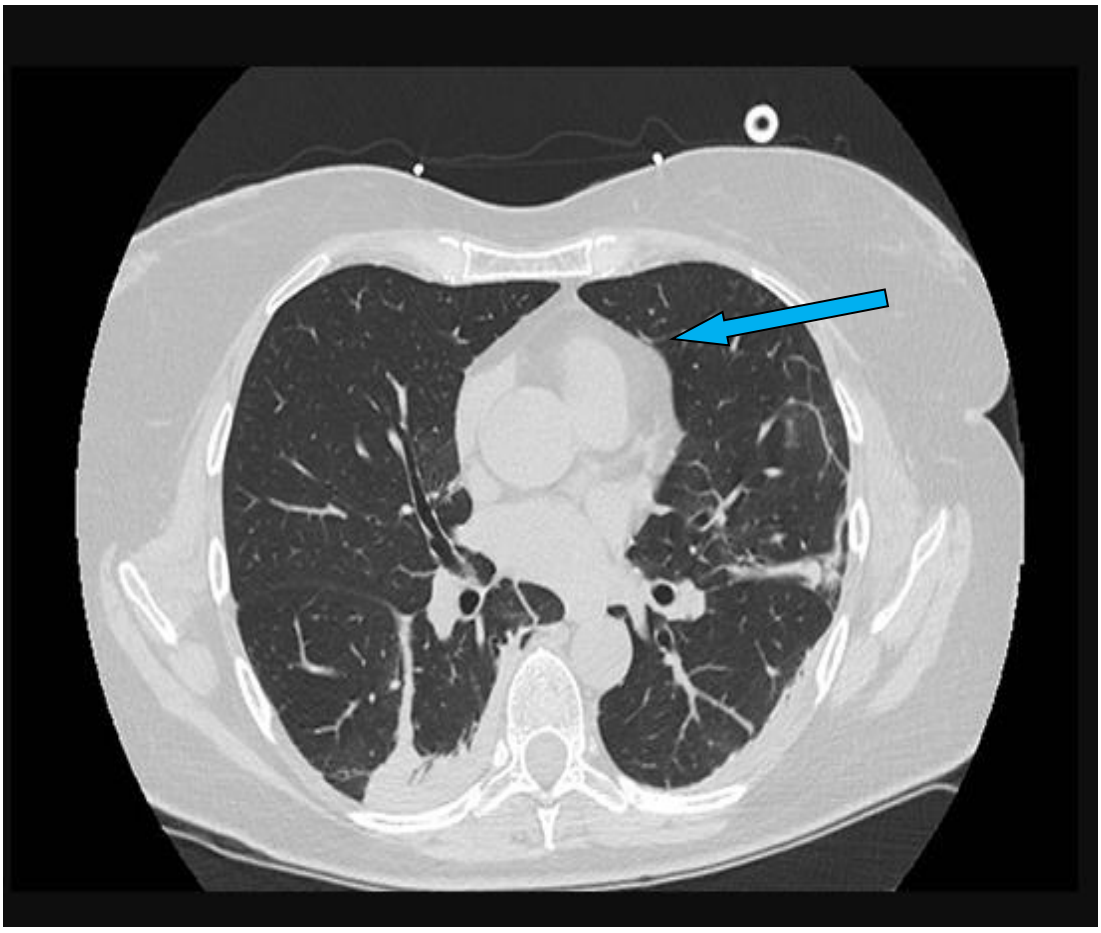


Figure 2.2 HRCT scan chest of COVID-19 patient at level of T4 vertebrae (radiologyinfo.org)

Arrow pointing towards peripheral ground glass lesion with consolidations

At the 3-month follow-up, 62 patients were available for pulmonary evaluation. The most frequent symptoms were dyspnea (46.7%) and cough (34.4%). Eighty-two percent of patients showed a lung diffusing capacity of less than 80%. The median distance in the 6MWT was 400 m (interquartile range, 362-440 m). CT scans showed abnormal results in 70.2% of patients, demonstrating reticular lesions in 49.1% and fibrotic patterns in 21.1%. Patients with more severe alterations on chest CT scan showed worse pulmonary function and presented more degrees of desaturation (Gonzaleze et al., 2021)

Most of the survivors had symptoms including fever, sputum production, fatigue, diarrhea, dyspnea, cough, chest tightness on exertion and palpitations in the three months after discharge. The serum troponin-I levels during the acute illness showed high correlation with the symptom of fatigue after hospital discharge (Liang et al., 2020)

Pulmonary restriction was associated with the degree of lung parenchymal involvement seen on CT scans during acute COVID-19, reflecting inflammation and fibrotic transformation following SARS-CoV-2 infection. Increasing evidence suggests a profibrotic phenotype following SARS-CoV-2 infection in line with other viral causes of pneumonia such as SARS, MERS and influenza infections. Post mortem analysis of lung tissue of lethal COVID-19 was reported to show ultra-structural alteration including alveolar collapse and fibrosis. Also, similarities in gene expression between idiopathic pulmonary fibrosis and COVID-19 in lungs of patients undergoing lung transplantations or post mortem analysis were found using single-cell RNA sequencing, including Keratin-17 expressing epithelial cells, profibrotic macrophages and myofibroblasts. Thus, analysis of CT scans during the acute phase may have prognostic relevance for patients. (Steinbeis et al., 2022)

OPERATIONAL DEFINITIONS

COVID 19

The coronavirus disease COVID-19 is a virus infection named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).(Barisione et al., 2020).

GROUND GLASS OPACITY

The initial abnormalities suggesting COVID-19 pneumonia on a chest radiograph are loss of the normal black appearance in the lung This is seen as increased whiteness, (because of increased density), but not enough to totally obscure lung markings; giving a ground glass appearance(Kanne et al., 2020)

CONSOLIDATION

Ground-glass opacities become denser and progress to consolidation with complete loss of lung markings.(Kovasc et al., 2020)

DISPLACEMENT OF HILUM OF LUNGS

Hilum of lung is a site where neurovascular bundles go in and out the lungs. It may displace in certain condition like consolidation or fibrosis which may interrupt the neurovascular supply. (Gianella et al., 2020)

SPIROMETRY

Spirometry assesses the integrated mechanical function of the lung, chest wall, respiratory muscles, and airway. (Miller et al., 2005)

PULMONARY FIBROSIS

Buildup of scar tissues in lungs is called pulmonary fibrosis. This can cause stiffness and collapse of lungs.(Gianella et al., 2020)

CT SCAN

A computerized tomography (CT) scan combines a series of X-ray images taken from different angles around the body and uses computer processing to create cross-sectional images (slices) of the bones, blood vessels and soft tissues inside the body.(Ramakrishna et al., 2004)

CHAPTER 3

METHODOLOGY

3.1 STUDY DESIGN

The research design for the research project “Chest Computed Tomography scan findings of lung and heart size after covid-19 pneumonia” was a case control study.

3.2 SUBJECTS

The proposed study was case control prospective research conducted on 42 subjects who were diagnosed with COVID 19 pneumonia three months before and now came for follow up and control group of same number who came for HRCT for anesthetic clearance for surgery but otherwise healthy no any . Detailed information was gathered in a pretested performa regarding severity of disease. Clinical findings were noted and HRCT performed.

3.3 SETTING

PNS Shifa hospital Karachi subjects coming for HRCT were taken as study participants.

3.4 INCLUSION CRITERIA

CASES- Survivors of COVID 19 discharged from hospital 3 months before and came for follow up CT scan

Age between 40-60 years

CONTROLS- Normal healthy individual who came for HRCT required for anesthetic clearance.

Age between 40-60 years

3.5 EXCLUSION CRITERIA

- The survivors of COVID 19 below 40 and above 60 years of age. Normal individual below 40 and above 60 years of age.
- Patient with pneumonia cause other than COVID 19 virus
- Patient with collapsed lung due to injury or trauma.
- Patient with previous cardiothoracic surgery

3.6 DURATION OF STUDY

Individual study period: 02 hours in radiology department of PNS Shifa

Total study period: 07 months

Data collection was started at PNS Shifa hospital, radiology department from month of September 2021 To March 2022.

Total duration of research was 07 months

3.7 SAMPLE SIZE ESTIMATION

The sample size was calculated to be 84

42 were cases who are survivors of COVID 19 admitted to hospital due to severity of disease and came for follow up HRCT after 03 months.

42 were normal healthy individual who came for HRCT for the anesthesia clearance before surgery.

3.8 SAMPLE SIZE CALCULATION

Sample size was drawn by taking in consideration the parameters used in article (Han et al., 2020)

Sample Size for Unmatched Case-Control Study

For:

Two-sided confidence level(1-alpha)	95
Power(% chance of detecting)	80
Ratio of Controls to Cases	1
Hypothetical proportion of controls with exposure	40
Hypothetical proportion of cases with exposure:	11.24
Least extreme Odds Ratio to be detected:	0.19

	Kelsey	**Fleiss**	**Fleiss with CC**
Sample Size – Cases	37	35	42
Sample Size – Controls	37	35	42
Total sample size:	74	70	84

References

Kelsey et al., Methods in Observational Epidemiology 2nd Edition, Table 12-15

Fleiss, Statistical Methods for Rates and Proportions, formulas 3.18 &3.19

CC = continuity correction

Results were rounded up to the nearest integer.

Print from the browser menu or select, copy, and paste to other programs.

3.9 SAMPLING TECHNIQUE

Non-probability convenient sampling

3.10 HUMAN SUBJECTS AND CONSENT

Human subjects with sever COVID 19 pneumonia admitted to hospital and discharged three months before this study. Now come for follow up with shortness of breath and fatigue. HRCT advised by pulmonologist

Second group is included subjects who are coming for HRCT for anesthesia clearance and otherwise healthy no any lungs pathology

A written informed consent was taken (Urdu and English)

3.11 MATERIALS USED

The materials which were used to conduct this study include consent forms i.e. English and Urdu, CT scan machine (Prime Aquilion-160 slice Toshiba), (Figure 3.2) CT reporting room, (Figure 3.3) CT scan reports and questionnaire.

The consent form and questionnaire are attached as Appendix C and D

3.12 PARAMETERS OF STUDY

The subject of this prospective study include the patients which were fulfilling the inclusion criteria after written informed consent and following were the parameters of the study

Age

Gender

Comorbidities

Length of stay in hospital due to COVID 19

Size of lungs on chest CT scan

The lobe of the lung involved most frequently

Displacement of hilum of lung

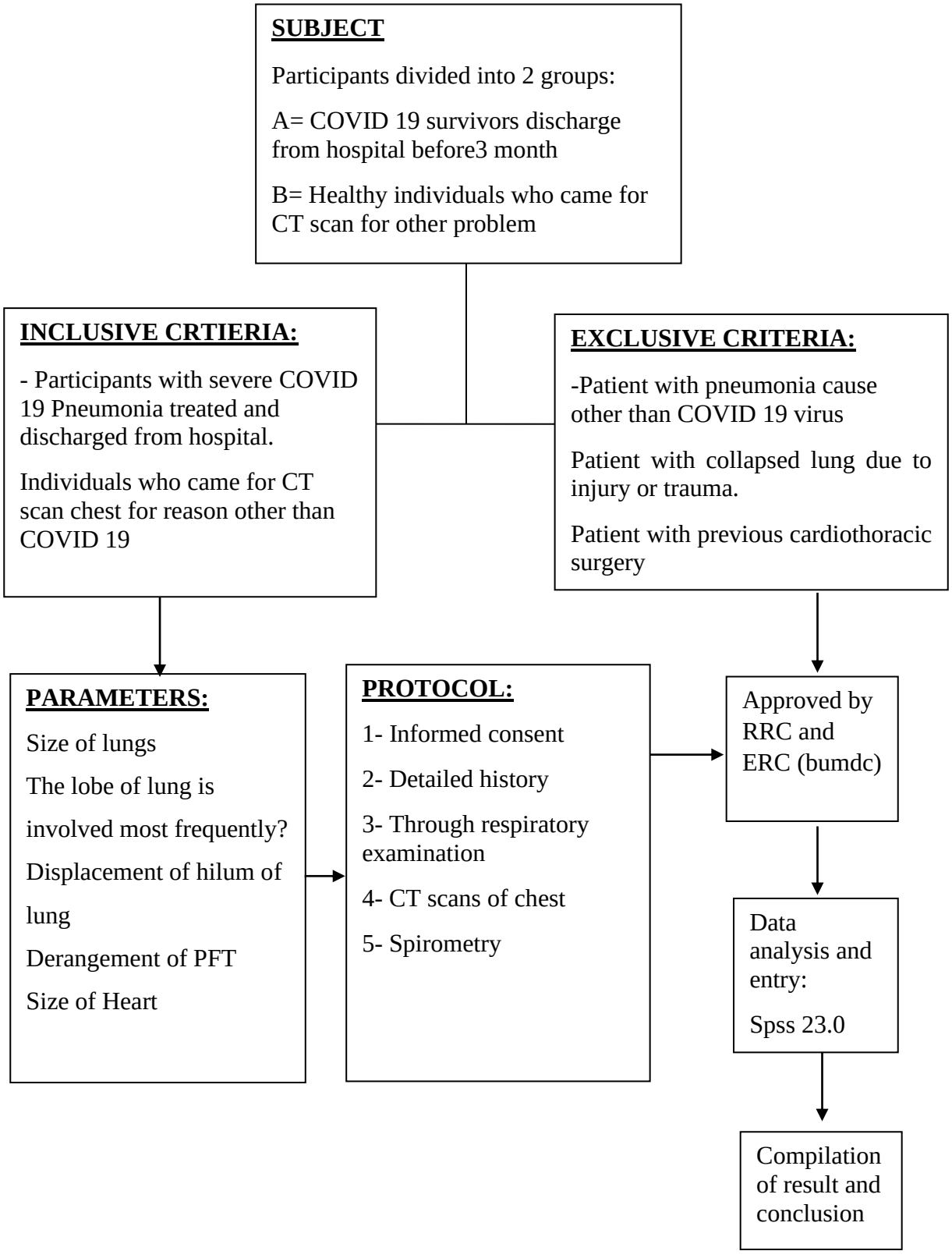
Size of Heart

3.13 PROTOCOL OF STUDY

The study was conducted after receiving ethical approval from ethical review committee (ERC) of Bahria University Medical and Dental Collage (BUMDC) Karachi. The date was collected at Radiology Department of PNS Shifa Hospital Karachi and duration of this study was six months. Subjects meeting the inclusion criteria were considered after written informed consent. Detailed history regarding their demographic data, age, and symptoms of COVID 19 and length of hospital stay was taken from all subjects.

After history taking and written informed consent, patients were prepared for CT scan of chest. CT scan machine of Prime Aquilion-160 slice of Toshiba Company was used. All CT-scan images were observed in CT reporting room of Radiology Department of PNS Shifa Hospital Karachi and lungs and heart measurements were taken.

3.14 FLOW CHART / ALGORITHM OF STUDY



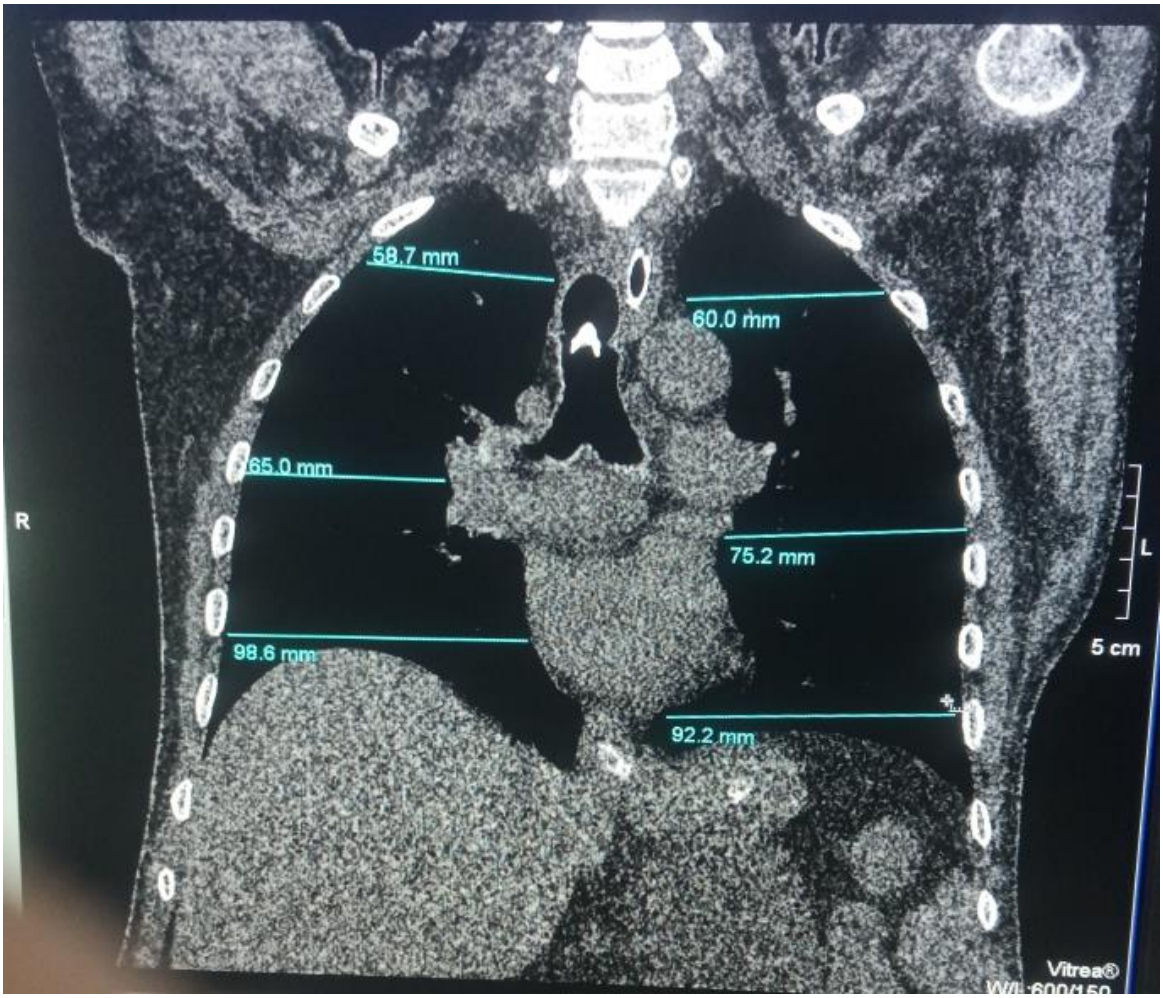


Figure 3.1 Measurement of lungs on chest CT scan
(FromResearch)

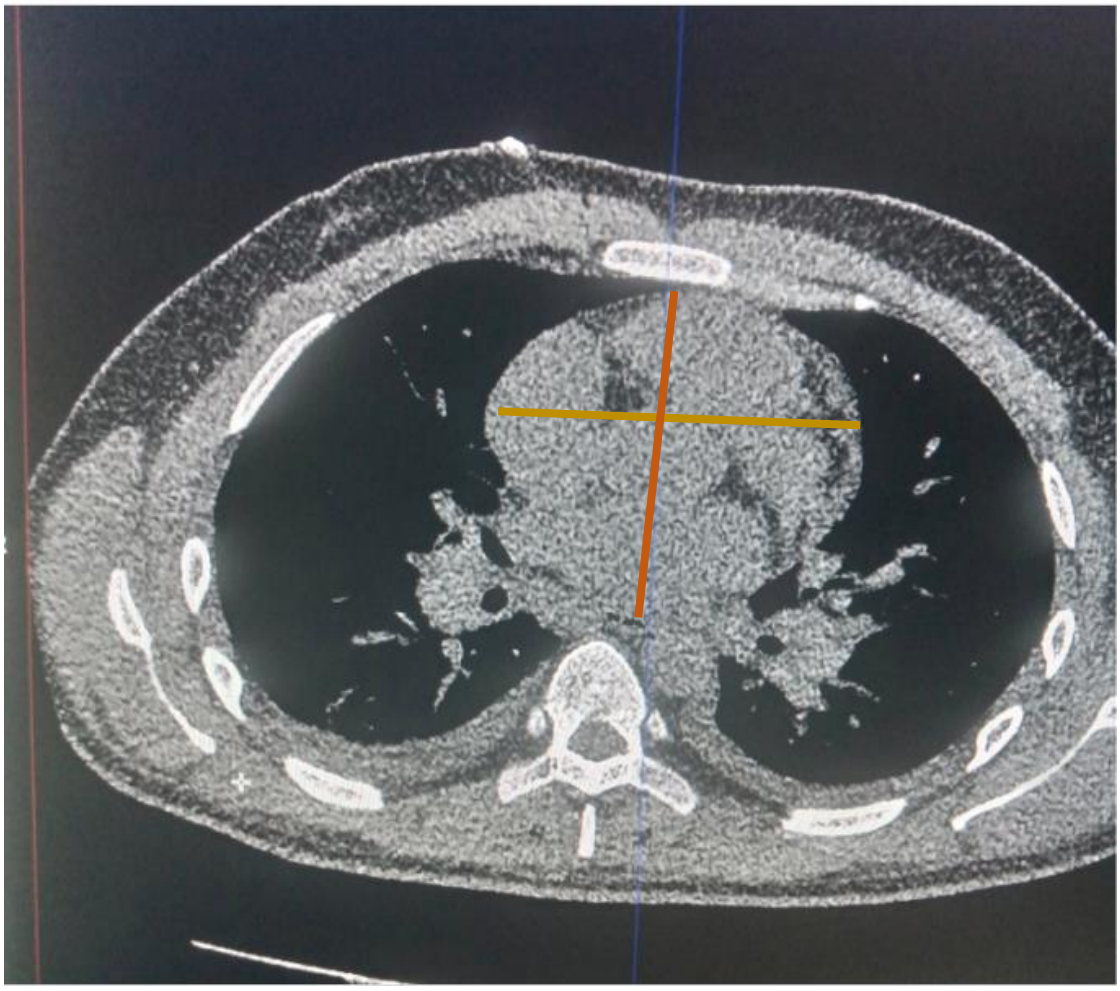


Figure 3.2 Measurement of heart size (From research)
Orange line: longitudinal Diameter
Yellow line: Transverse diameter

Figure 3.3 CT scan machine (Prime Aquilion-160 slice Toshiba)

(From Research)

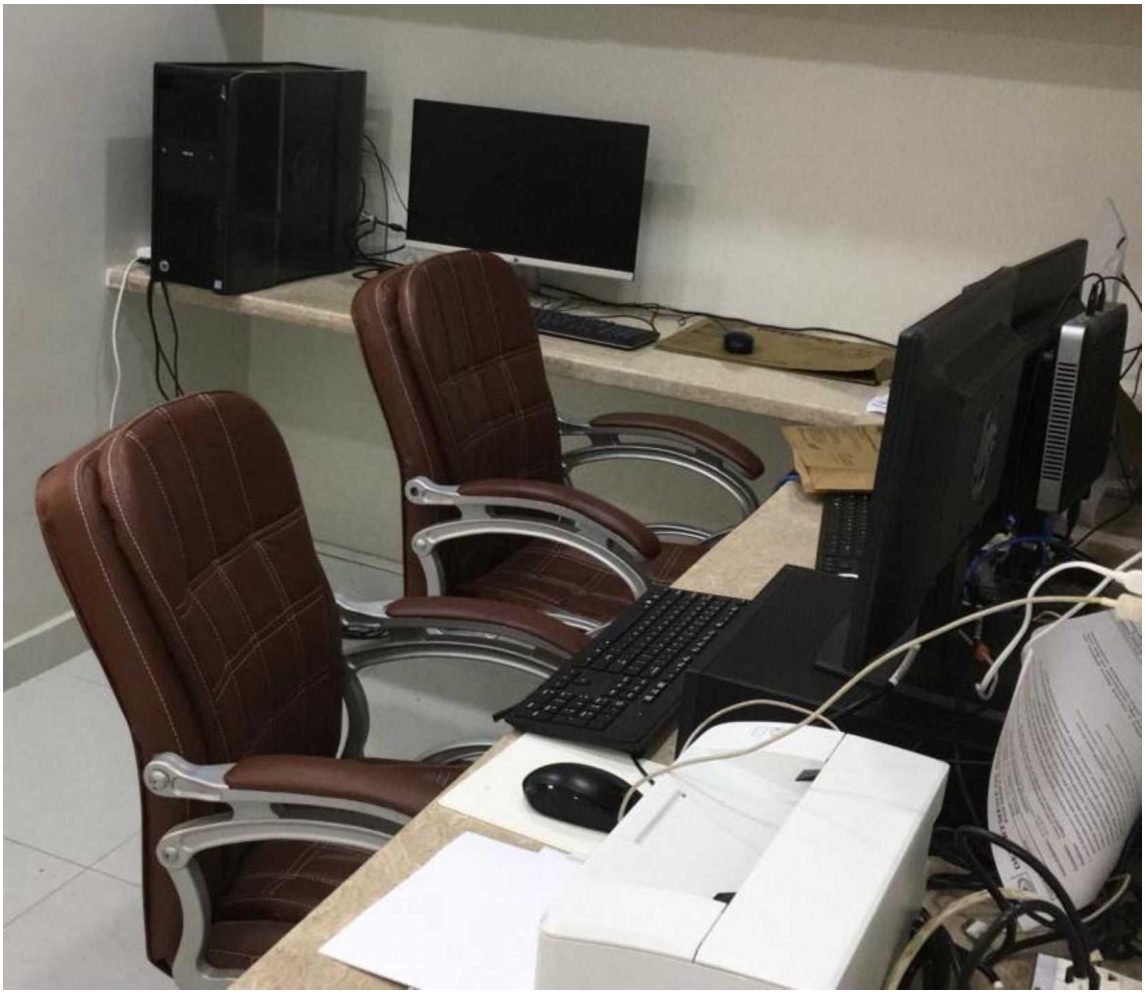


Figure 3.4 CT reporting room

(From Research)

3.15 STATISTICAL ANALYSIS

Statistical analysis was done using the statistical package for social science (SPSS) software version 23.0.The data was found to be non-parametric by using Kolmogorov-Smirnova test. Test applied to observe correlation Wilcoxon test. Test applied to observe significance: Mann-Whitney U Test. The p-value<0.05 was considered as statistically significant.

CHAPTER 4

RESULTS

BASELINE DEMOGRAPHIC CHARACTERESTICS

GEDER DISTRIBUTION OF PARTICIPANTS

A total of 82 participants of study 42 were cases along with control group of 42 subjects. Research was conducted at Radiology department of PNS Shifa hospital. It was found that among cases majority of patients were male 30 whereas 12 were female. Among control group 24 were male and 18 were female.

RESULT FOR PERSONAL HISTORY QUESTIONS

ILL HABITS CONSUMPTION

The subjects were inquired about smoking habits. It was observed the out of 42 cases 21 were smoker and 21 were nonsmokers. The dietary habits were good.

COMPARISION OF SAGITTAL DIAMETER OF RIGHT LUNG OF CASES AND CONTROL

The sagittal diameter of right lungs were measured of both cases and healthy controls and it showed reduced sagittal diameter of cases as compared to controls with mean 63.38 and p value was significant (0.000)(Table 4.1)

COMPARISION OF CORONAL DIAMETER OF RIGHT LUNG OF CASES AND CONTROL

In the current study coronal diameter of right lungs was measured of cases and controls and it showed shrunken lungs and reduced coronal diameter of cases with mean21.50 as compared to controls with mean 63.50 and p value is significant (0.000)(Table 4.1)

COMPARISION OF AXIAL DIAMETER OF RIGHT LUNG OF CASES AND CONTROL

The CT scan of enrolled subjects were also evaluated for axial diameter of right lungs and axial diameter of cases was less as compared to controls with mean 63.24 and p value was significant(0.000)(Table 4.1)

COMPARISION OF CORONAL DIAMETER OF LEFT LUNG OF CASES AND CONTROL

The CT scan of 42 cases also showed reduced coronal diameter of left lung of cases with mean 22.19 as compared to controls with mean 62.81 and p value was significant (0.000)(Table 4.2)

COMPARISION OF SAGITTAL DIAMETER OF LEFT LUNG OF CASES AND CONTROL

This study include CT scan of 42 cases and 42 subjects and measure the sagittal diameter of left lungs and it showed shrunken lungs of cases and reduce the sagittal diameter of cases with mean 21.50 as compared to controls with mean 63.50 and p value was significant(0.000) (Table 4.2)

COMPARISION OF AXIAL DIAMETER OF LEFT LUNG OF CASES AND CONTROL

This study include CT scan of 42 cases and 42 subjects and measure the axial diameter of left lungs and it showed shrunken lungs of cases and reduce the axial diameter of cases with mean 21.50 as compared to controls with mean 63.50 and p value was significant(0.000)(Table 4.2)

COMPARISION OF HEART SIZES OF CASES AND CONTROL

When heart sizes of COVID 19 follow up cases and healthy subjects were compared on CT scan it was found the transverse diameter of heart of cases was significantly more than the subjects showing significant p value. There was no significant difference between the longitudinal diameters of heart of both groups. It was 51.04 in cases and 33.96 in controls. (Table 4.3)

COMPARISION OF SMOKING HABIT WITH LENGTH OF HOSPITAL STAY AND OXYGEN REQUIREMENTS

Association of smoking was compared with length of hospital stay and oxygen requirement. This did not affect the length of stay in hospital and average length of stay in hospital is same for both but smokers required oxygen support during hospital stay (Table 4.4)

COMPARISION OF COMORBIDITIES WITH HOSPITAL STAY AND OXYGEN REQUIREMENTS

In this case control study 42 cases were inquired about the comorbidities and the most common finding was hypertension and 19 cases were reported as hypertensive over 5 years and 23 were non hypertensive. Time duration of hospitalization was 5-6 days more for hypertensive patient as compared to non-hypertensive. (Table 4.5) Oxygen support is required for hypertensive patients as compared to non-hypertensive with significant p value (Table 4.5)

EFFECT OF SMOKING ON LUNGS ON CT SCAN

There was no significant difference observed on diameter of lungs at CT scan of COVID 19 follow up patients who were smokers and non-smokers with non-significant p value. (Table 4.6, 4.7)

COMPARISON OF TRANSVERSE AND LONGITUDINAL DIAMETER OF HEART BETWEEN SMOKER AND NON-SMOKER

The diameter of heart at CT scan of COVID 19 follow up patients who were smokers and non-smokers compared and no significant results found with insignificant p value. (Table 4.8)

ICU ADMISSION OF SMOKERS AND NON-SMOKERS

The requirement of ICU admission for smokers is 35.0% and13.6% non-smokers require ICU admission. Comparatively 65.0% of smoker and 86.4% of non-smokers require no ICU admission during hospital stay which showed no significant difference between smokers and non-smokers ICU admission. (Table 4.9)

ICU ADMISSION OF CASES WITH COMORBIDITIES

Admission of ICU was compared in hypertensive and non-hypertensive cases and no significant result was found. (Table 4.12)

CORRELATION OF AGE WITH LENGTH OF HOSPITAL STAY, DIAMETERS OF BOTH LUNGS AND HEART

By using spearman rho test the correlation of age with hospital stay was identified results shows positive correlations of these two parameters. It was also observed that sagittal diameter of both lungs, axial and coronal diameter of right lung and diameters of heart have negative association with age which indicate increasing age did not affects these parameters. Coronal and axial diameter of left lung shows positive correlation with age which means these parameters are affected by increase age (Table 4.13)

Table 4.1 Comparisons of sagittal, coronal and axial diameter of right lung between the cases and control group

	Group	N	Mean (mm)	p-value
Sagittal diameter Right Lung	Case	42	21.62	0.000**
	Control	42	63.38	
	Total	84		
Coronal diameter Right Lung	Case	42	21.50	0.000**
	Control	42	63.50	
	Total	84		
Axial diameter Right Lung	Case	42	21.76	0.000**
	Control	42	63.24	
	Total	84		

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

Table 4.2 Comparison of sagittal, coronal and axial diameter of left lung between the cases and control group

	Group	N	Mean (mm)	p-value
Sagittal diameter Left Lung	Case	42	21.50	0.000**
	Control	42	63.50	
Coronal diameter Left Lung	Case	42	22.19	0.000**
	Control	42	62.81	
Axial diameter Left Lung	Case	42	21.50	0.000**
	Control	42	63.50	

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

Table 4.3 Comparison of transverse and longitudinal diameter of heart between the cases and control group

	Group	N	Mean	p-value
Transverse diameter	Case	42	51.04	0.001*
	Control	42	33.96	
	Total	84		
longitudinal diameter	Case	42	46.74	0.111
	Control	42	38.26	
	Total	84		

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

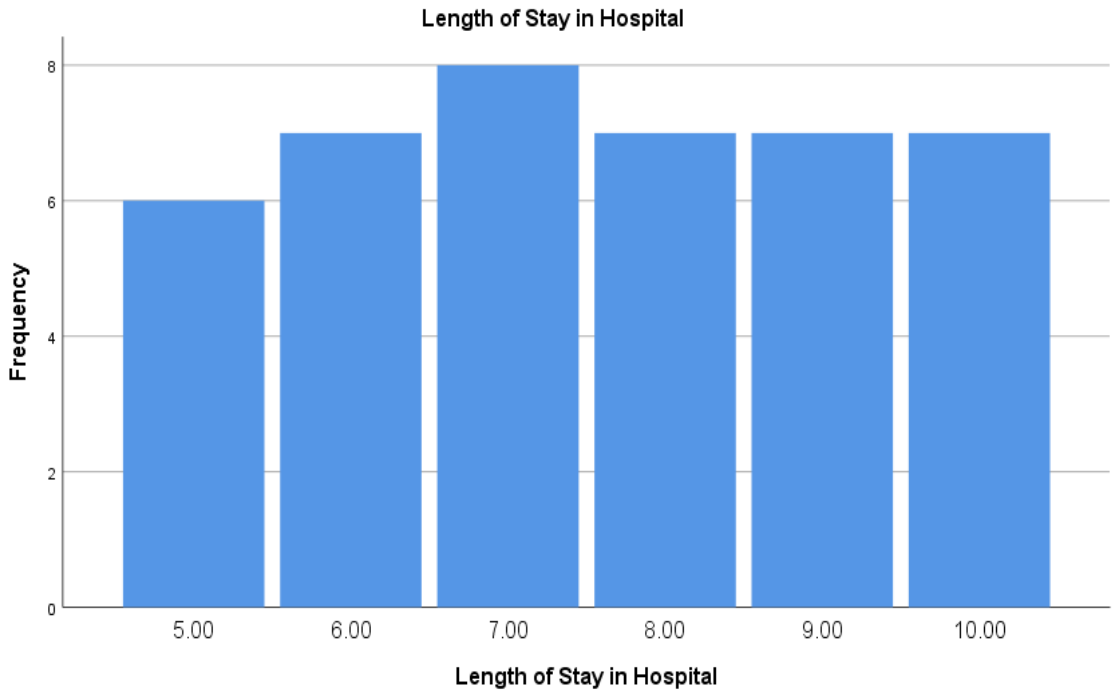


Figure 4.1 Bar graph shows length of hospital stay
Horizontal: Number of days
Vertical: Number of patients

Table 4.4 Comparison of length of stay in hospital between smoker and non-smoker

	Smoking	N	Mean	p-value
Length of Stay in Hospital	Smoker	20	22.63	0.566
	Non Smoker	22	20.48	
	Total	42		

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

Table 4.5 Comparison of length of stay in hospital between hypertensive and non-hypertensive

	Hypertension	N	Mean	p-value
Length of Stay in Hospital	Yes	19	25.95	0.030*
	No	23	17.83	
	Total	42		

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

Table 4.6 Sagittal, coronal and axial diameter of right lung of smoker and non-smoker

	Smoking	N	Mean Diameter	p-value
Sagittal diameter Right Lung	Smoker	20	22.50	0.614
	Non Smoker	22	20.59	
Coronal diameter Right Lung	Smoker	20	19.93	0.426
	Non Smoker	22	22.93	
Axial diameter Right Lung	Smoker	20	18.30	0.106
	Non Smoker	22	24.41	

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

Table 4.7 Sagittal, coronal and axial diameter of left lung of smoker and non-smoker

	Smoking	N	Mean	p-value
Sagittal diameter Left Lung	Smoker	20	24.30	0.156
	Non Smoker	22	18.95	
Coronal diameter Left Lung	Smoker	20	21.60	0.160
	Non Smoker	22	21.41	
Axial diameter Left Lung	Smoker	20	19.03	0.210
	Non Smoker	22	23.75	

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

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Table-4.8: Comparison of transverse and longitudinal diameter of heart between smoker and non-smoker

	Smoking	N	Mean Diameter	p-value
Transverse diameter	Smoker	20	24.30	0.157
	Non Smoker	22	18.95	
	Total	42		
Longitudinal diameter	Smoker	20	22.40	0.650
	Non Smoker	22	20.68	
	Total	42		

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

Table-4.9: ICU admission of smokers and non-smokers

		Smoking		p-value
		Smoker	Non smoker	
ICU admission	Yes	7	3	0.104
		35.0%	13.6%	
	No	13	19	
		65.0%	86.4%	

Key:
p-value ≤0.05: Significant*
Chi-Square Test was applied to see significance

Table 4.10 Oxygen requirement of smoker and non-smoker

		Smoking		p-value
		Smoker	Non smoker	
Oxygen requirement	YES	14	9	0.059
		70.0%	40.9%	
	NO	6	13	
		30.0%	59.1%	

Key:
p-value ≤0.05: Significant*
Chi-Square Test was applied to see significance

Table 4.11 Oxygen requirement of hypertensive and non-hypertensive patients

		Hypertension			p-value
		Yes	No	Total	
Oxygen Requirement	Yes	17	6	23	0.000**
		89.5%	26.1%	54.8%	
	No	2	17	19	
		10.5%	73.9%	45.2%	

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

Table-4.12: ICU admission of cases with comorbidities

		Hypertension			p-value
		Yes	No	Total	
ICU admission	Yes	7	3	10	0.071
		36.8%	13.0%	23.8%	
	No	12	20	32	
		63.2%	87.0%	76.2%	

Key:
p-value ≤0.05: Significant*
Chi-Square Test was applied to see significance

Table-4.13: Correlation of age with sagittal, axial and coronal diameter of left and right lungs

	Correlation Coefficient	p-value
Age , Length of stay in hospital	0.147	0.000**
Age, Sagittal diameter of right lung	-0.040	0.801
Age , Coronal diameter of right lung	-0.102	0.522
Age, Axial diameter of right lung	-0.038	0.811
Age, Sagittal diameter Left Lung	-0.057	0.719
Age, Coronal diameter Left Lung	0.152	0.335
Age, Axial diameter Left Lung	0.086	0.590
Age, Transverse diameter of heart	-0.057	0.719
Age, longitudinal diameter of heart	-0.048	0.764

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Spearman's rho test was applied to see significance

Table 4.14 Fibrosis present in hypertensive patients

		Fibrosis		p-value
		Present	Absent	
Hypertension	Yes	64.0%	17.6%	0.003*
	No	36.0%	82.4%	

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

Table 4.15 Oxygen requirements for patient with fibrosis

		Fibrosis		p-value
		Present	Absent	
Oxygen requirement	Yes	72.0%	29.4%	0.006*
	No	28.0%	70.6%	

Key:
p-value ≤0.05: Significant*
p-value ≤ 0.001: Highly significant**
Mann-Whitney U Test was applied to observe significance.

CHAPTER 4

DISCUSSION

In the present study entitled “Chest CT scan findings of lung and heart size after COVID-19 pneumonia” we aimed to investigate changes in the size of lungs and heart on follow up computed tomography (CT) scan in patients with coronavirus disease 2019 COVID-19. Patients who underwent chest CT scan and symptom assessment, three months after discharge from the hospital were enrolled. We measured the size of heart and lung on CT scan of COVID 19 survivors collecting the information regarding long term effects of the disease which may be helpful in planning management of COVID 19 pneumonia as fibrotic changes of lungs may have effected pulmonary function tests resulting in breathing problems.

Literature search shows that symptoms like dyspnea and fatigue persist even after three months of hospital discharge and radiological abnormalities persist at follow up of COVID 19 patients even after 3,6 and 12 months. Most frequent CT findings of COVID follow up patient were fibrosis and ground glass opacities. Both lungs were equally involved with fibrosis and ground glass opacities more prominent at lower lobes. Medium term follow up at three months of patients diagnosed with SARS Covid pneumonia showed the persistence of abnormalities in CT scans, a significant functional impairment assessed by lung function tests and a decreased quality of life in affected patients. Further studies evaluating long term impact are warranted to guarantee an appropriate follow up to patients recovering from SARS COV 2 pneumonia. (Gianella et al., 2021)

This present study also showed fibrosis in both lungs with shrunken lungs and reduced the lung sizes which have significantly affected pulmonary function causing dyspnea. At the 3-month follow-up, the most frequent symptoms were dyspnea and cough. During this time span patients showed less lung diffusing capacity. CT scans showed abnormal results, demonstrating reticular lesions with fibrotic patterns. Patients with more severe alterations on chest CT scan showed worse pulmonary function and desaturation. Factors associated with the severity of lung damage on chest CT scan were age, length of the ICU stay and duration of invasive mechanical ventilation. Three months after hospital discharge, pulmonary structural abnormalities and functional impairment are highly prevalent in patients with ARDS secondary to COVID-19 who required an ICU stay. It is determined that after three months of discharge pulmonary evaluation should be considered for all critical COVID-19 survivors. (Gonzalez et al., 2021)

With the intention of identifying and timely managing respiratory complications from COVID-19, current recommendations state that patients who suffered from severe COVID-19 pneumonia should undergo a clinical and radiological assessment at 12 weeks after discharge.

In the present study, a significant proportion of such patients still had physiologically relevant CT abnormalities, further highlighting the need for follow-up strategies to support COVID-19 survivors through the recovery phase. The most common CT findings were GGO admixed with reticulation and linear opacities (i.e. Parenchymal bands and sub pleural curvilinear lines), along with signs of architectural distortion and bronchial dilatation. The percentage of lung involvement correlated with dyspnea severity and cough. As COVID 19 virus effect is multi organs, current study also focused the diameters of heart on chest CT scan and compared with normal individual’s heart which showed significant results.

Xie et al (2020) analyzed the chest CT findings of 99 patients with COVID-19 and observed that 25% of the patients presented with unilateral lung lesions and 75% with bilateral lung lesions, consistent with the present study findings. The result of this study also shows fibrosis of both lungs involving each lobe but more prominently lower lobes reducing lung sizes as compared to healthy individual after three months of discharge.

Wu et al (2021) states that CT scan findings were subjected to visual scoring based on the proportion of patchy ground-glass opacities and lung consolidations results showing that the scores of the both lungs were significantly higher in the severe group of COVID 19 survivors than in the moderate group, suggesting that the severe group had higher area proportions of ground-glass opacities and lung consolidations in the lung lobes than those in the moderate group, and, thus, would require a longer recovery time. The present follow-up study also shows that CT findings were subjected to semi quantitative scoring based on the proportion of fibrotic lesions results showed that the involvement of left lung, the right lung, and both lungs were all significant in the cases than in the control group, suggesting that the COVID 19 survivors had higher area of fibrotic lesions and require further management.

COVID-19 SEVERITY GROUPS-CDC GUIDELINES

Asymptomatic/ presymptomatic	**Positive for SARS-COV 2 using a test but no symptoms that are consistent with COVID-19**
Mild illness	**Signs and symptoms of COVID-19 but there is no shortness of breath, dyspnea or abnormal chest imaging**
Moderate illness	**Signs and symptoms of lower respiratory disease or abnormal imaging and Spo2≥ 94% on room air at sea level**
Sever illness	**Spo2 <94% on room air at sea level. Pao2/Fio2<300mm mercury, respiratory frequency 30 beats per minutes**
Critical illness	**Respiratory failure, septic shock and multiple organ dysfunction**

Patients with lung fibrosis showed a higher incidence of ARDS (63%), which was also a predictor of fibrosis of lungs. Previous studies demonstrated that a substantial proportion of patients who survived ARDS may develop progressive fibrotic-like changes on CT scans. Nevertheless, it remains uncertain whether the fibrotic changes observed in this study represent true fibrotic lung disease (e.g. at pathology or on longer term follow-up CT). Whether or not these changes, found at 3 months, reflect permanent change in the lung remains to be investigated. Additionally, the high frequency of non-invasive mechanical ventilation is another risk factor for the development of fibrotic at 3 months in our study. Based on previously published data, mechanical ventilation was strongly related to fibrosis observed after ARDS. Likewise, the lung fibrotic changes in our patients may also be associated with ventilator induced lung injury. Emerging evidence of coagulopathy and an over exuberant inflammatory response has been reported in severe COVID-19 patients, which are associated with disease severity and may also lead to greater damage to the pulmonary parenchyma (Xiong et al., 2021) It was found that a higher CT score (≥18) on the initial CT was an independent prognostic factor for the presence of fibrosis on the 3 months follow up exam. According to a previous study on idiopathic pulmonary fibrosis CT score was correlated with the degree in pathological specimens. Moreover, a recent research revealed an association between a CT score of ≥ 18 with an increased mortality risk in COVID-19 patients. Therefore, a greater extent of lung injury in the acute phase may be associated with a higher mortality rate and more severe pulmonary sequelae in survivors. In addition, the correlations of scores for fibrotic changes with the aforementioned risk factors were also confirmed in our study. (Thoma et al., 2009) At the three month follow-up, a few patients still complained of ongoing respiratory symptoms and 26% of patients had pulmonary diffusion abnormalities, which occurred more frequently occurred in patients with lung fibrosis. Thus, both structural and functional lung impairments may simultaneously occur in patients who survive severe COVID-19 pneumonia (Oudkerk et al., 2020)

Two studies reported an increased extension of the GGO or consolidation and a decreased density on follow up CT scan of COVID-19 pneumonia, which may indicate the gradual regression of the inflammation and re-expansion of the alveoli. GGO in the acute phase of COVID-19 pneumonia may represent the inflammatory infiltrates, edema or hemorrhaging (Liu et al., 2020; Xu et al., 2020).

In a recent SARS-CoV-2 outbreak, the rate of radiologic abnormalities remained high3 months after discharge (74.55%), although it was lower than that at the time of admission (84%) (Xiaong et al., 2021)

A study also performed at the 3-month follow-up of COVID 19 survivors who were previously admitted in ICU for COVID 19 showed that fibrosis was present in 23.6% of patients with abnormal CT scan findings (YM et al., 2020)

As COVID 19 virus effect is multi organs, current study also focus the diameters of heart on chest CT scan and compared with normal individual's heart which shows significant results.

SARS-CoV-2, the causative agent of COVID-19, has been shown to cause persistent damage of the heart, intestine, kidney and pulmonary system by a direct effect owing to viral replication in the organ cells and indirect damage secondary to respiratory failure or an exaggerated immune system response (Bohme al., 2020)

That damage induces symptoms in the acute stage, and may also in the sequel stage. A previous study revealed cardiac involvement in 78% of German patients recovered from COVID-19 and ongoing myocardial inflammation in 60% of all patients, independent of preexisting conditions, severity and overall course of the acute illness, and time from the original diagnosis, which indicates COVID-19 can cause persistent damage even in the sequel stage (Puntmann et al., 2020).

Current study also states that there is long term effect of COVID 19 on heart and result showed reduced transverse diameter of heart on CT scan chest of COVID 19 survivors then the control group. Previous studies showed that myocardial injury occurs in a significant proportion of COVID-19 patients and the cardiac TNI or troponin-T which is the sensitive marker of myocardial injury and an independent predictor of clinical outcomes in the acute stage is also associated with heart damage in the recovery stage of COVID-19 (Huang, Wang, Li et al., 2020)

Multiple studies have demonstrated that myocardial injury, characterized by elevation in serum cardiac biomarkers, is common in COVID-19. The prevalence of myocardial injury, however, is variably reported, with early studies quoting a prevalence of 8–12% in hospitalized patients, whilst more recent data suggests that it is possibly much higher (Bansal et al., 2020, Kevin et al., 2020) subsequently, a larger multicenter study of 305 patients identified an elevated troponin in more than half of the

hospitalized patients. A recent German cohort study reported imaging evidence of myocardial injury by cardiovascular magnetic resonance (CMR) in over 70%, although whether this was pre-existing or consequence was unclear with single time-point imaging.(Glustino et al., 2020)(Gorecka et al., 2020)

A significant proportion of patients presenting with COVID-19 infection requiring hospitalization have evidence of myocardial injury based on serum cardiac troponin elevations, with an incidence ranging from 7% to 40% (Guo et al., 2020, Lippi et al., 2020). In most prior studies, cardiac injury has been associated with increased risk of in-hospital complications and mortality. However, the underlying mechanisms of myocardial injury in patients with COVID-19 remain poorly understood because prior studies have not included cardiovascular imaging data and troponin elevations per se do not differentiate between etiologies of myocardial damage. In the present study, we comprehensively characterized the structural cardiac abnormalities of patients with COVID-19 infection by measuring the heart size on CT scan chest. The result shows the increase heart sizes which denote significant myocardial injury. (Giustino et al., 2020)

Myocardial injury seems to correlate with the severity of the clinical manifestations of COVID-19 and may identify patients with worse baseline clinical status. COVID-19 has been shown to broadly affect the cardiovascular system (Atri et al., 2020) (Guistino et al., 2020). Proposed mechanisms include cytokine mediated myocardial damage, oxygen supply demand imbalance, microvascular and macrovascular thrombosis, endothelial damage, and possibly direct viral invasion of the myocardium (Bavishi et al., 2020). It is therefore possible that the cardiac damage resulting from COVID-19, through direct or indirect pathways, contributes to the poor prognosis observed in certain patients. Acute myocardial infarction is a leading cause of death worldwide and a treatable and recognizable cause of irreversible cardiac damage (Thygesin et al., 2020).

In summary, follow-up CT scans obtained within 3 months of disease onset showed fibrotic-like changes in the lung in more than one-third of patients and also affect the diameter of heart who survived severe coronavirus disease 2019 pneumonia. These patients were older and had more severe disease during the acute phase. However, the long-term lung sequelae of these CT findings are still largely unknown. This report serves as a basis for new, prospective, large-scale, long-term investigations analyzing these high-risk patients.

Patients with COVID-19 and myocardial injury have a broad spectrum of cardiac abnormalities, although approximately one-third of such patients show no evidence of structural cardiac disease. Myocardial injury is associated with increased risk of in hospital mortality particularly in the presence of cardiac structural abnormalities.

CHAPTER 6

CONCLUSION

6.1 CONCLUSION OF STUDY

On the basis of this study, it can be concluded that corona virus may cause lung injury and fibrosis which shrinks the size of lungs. The HRCT scan at three month-follow up of patients with COVID 19 disease who were admitted in hospital for 8 to 10 day-duration revealed fibrotic changes and sagittal, coronal and axial diameter of lungs were reduced as compared to CT scan chest of healthy controls. Increasing age, comorbidities and smoking increase severity of lung damage.

The diameter of heart was also found increased on chest HRCT scan at three month- follow up of COVID 19 patients as compared to controls.

6.2 RECOMMENDATIONS

- It is recommended that Spirometry should also be done at three month follow up of COVID 19 patients
- Oxygen therapy should be given at earlier stages of COVID 19 pneumonia to reduce the lung complications
- The follow up of patients with COVID 19 should be done at six months and one year as injury persists for long time

- In COVID 19 patients cardiac enzymes and echocardiography should be carried out along with chest CT scan for evaluation of virus effect on the heart.

6.3 STRENGTH OF STUDY

- This is the pioneer study in Pakistan conducted on a new disease
- This study focused on follow up of COVID 19 patients so that long term effect of this contagious disease is highlighted
- This study showed the importance of CT scan at follow up visits of patients
- This study correlated the hypertension and smoking habit with the severity of disease which should be added for counseling

6.4 LIMITATION OF STUDY

- Large number of cases and multicenter options must be taken in order to authenticate study further.
- All parameters of lung and heart injury were not measured
- Spirometry, echocardiography and cardiac enzymes should be done at follow up for more information regarding

CHAPTER 7

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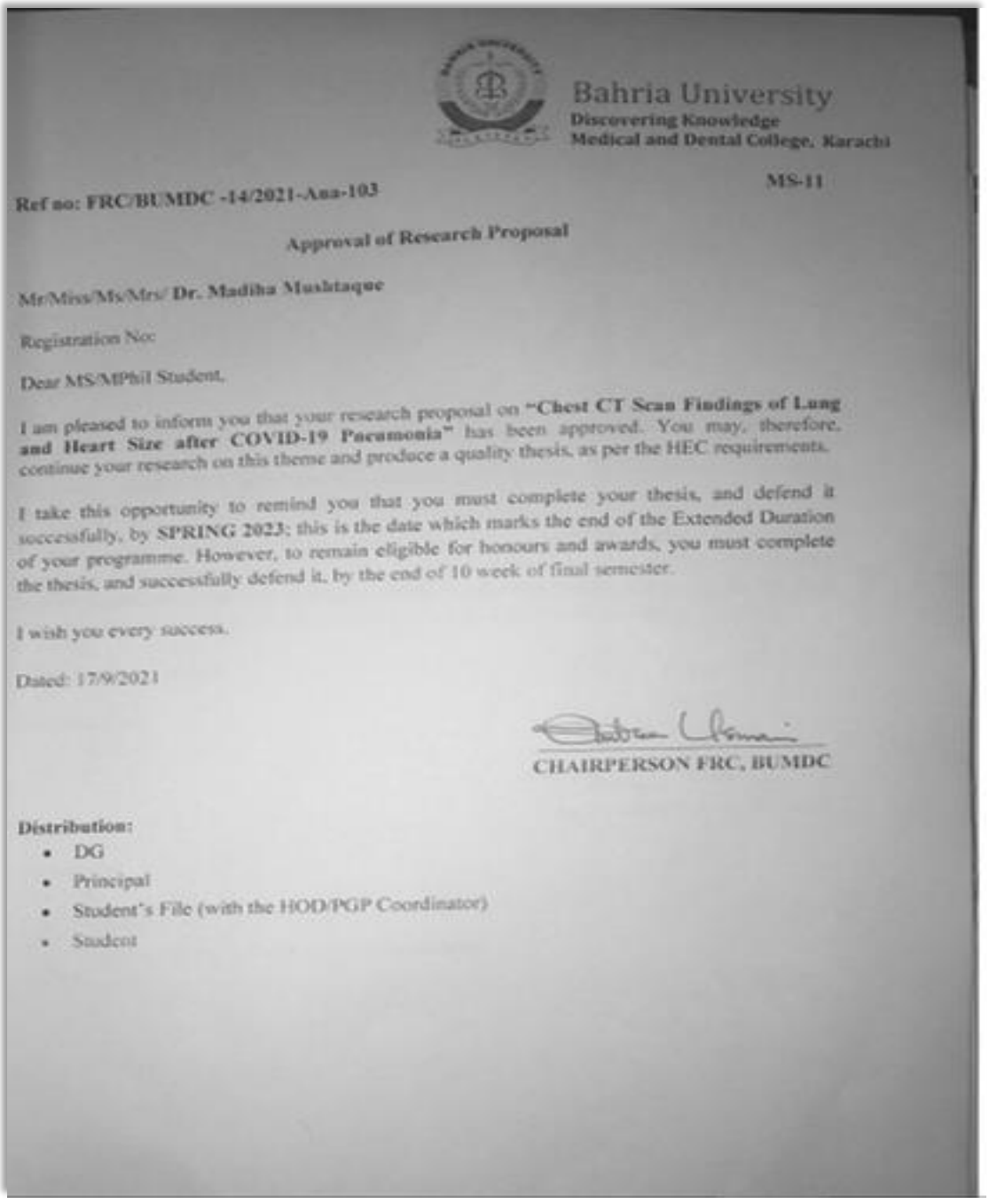
CHAPTER 8

APPENDICES

(A) BUMDC- FRC Approval letter



Bahria University
Discovering Knowledge
Medical and Dental College, Karachi

MS-11

Ref no: FRC/BUMDC -14/2021-Ana-103

Approval of Research Proposal

Mr/Miss/Ms/Mrs/ **Dr. Madiha Mushtaque**

Registration No:

Dear MS/MPhil Student,

I am pleased to inform you that your research proposal on **"Chest CT Scan Findings of Lung and Heart Size after COVID-19 Pneumonia"** has been approved. You may, therefore, continue your research on this theme and produce a quality thesis, as per the HEC requirements.

I take this opportunity to remind you that you must complete your thesis, and defend it successfully, by **SPRING 2023**; this is the date which marks the end of the Extended Duration of your programme. However, to remain eligible for honours and awards, you must complete the thesis, and successfully defend it, by the end of 10 week of final semester.

I wish you every success.

Dated: 17/9/2021

CHAIRPERSON FRC, BUMDC

Distribution:

- DG
- Principal
- Student's File (with the HOD/PGP Coordinator)
- Student

(B) BUMDC -ERC Approval letter

Bahria University
Discovering Knowledge
Medical and Dental College Karachi

ETHICAL REVIEW COMMITTEE
LETTER OF APPROVAL

Date: 21-Dec-21

FRC Reference:
FRC/BUMDC-14/2021-Ana-103

PATRON
Prof. Ambreen Usmani
Principal & Dean
Health Sciences(BU)

CHAIRPERSON
Dr. Quratulain Javaid

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Prof Reza H Syed
Ms Shabina Arif
Mr M Amir Sultan

Dr. Madiha Mushtaque
MPhil Student
Department of Anatomy
BUHS-Karachi

Subject: Institutional approval of research study

Title of Study: Chest CT Scan Findings of Lung and Heart Size after COVID-19 Pneumonia

Principal Investigator: Dr. Madiha Mushtaque

Reference No: ERC 88 /2021

Dear Dr. Madiha Mushtaque,

Thank you for submitting the above mentioned study proposal. ERC Bahria University Medical and Dental College has reviewed this project in the meeting held on 21-December-2021 and gives approval. Kindly notify us when the research is complete.

Regards,

21/12/21
DR. AMBREEN SURTI
Secretary, ERC
BUMDC

21/12/21
DR. QURATULAIN JAVAID
Chairperson, ERC
BUMDC

Cc:
DG-BUMDC
Principal BUMDC

(C) WRITTEN INFORMED CONSENT FORM OF PATIENT

I am giving my consent to participate voluntarily and at my own will in the research project that aims for the morphological variations in lungs after COVID 19 pneumonia. The project will evaluate the changes that will help in the future in prevention and treatment procedure of COVID 1.

I have been explained in detail the nature and significance of participating in the project that analysis lungs and heart abnormalities and sizes will help me in follow up treatment plan of COVID 19. In case of fibrosis and changes in sizes of lungs it can cause dyspnea and cough. I understand the provided explanation.

I have been told that all the findings and my personal data will be kept strictly confidential and will be used only for the benefit of pulmonologist to make treatment plan so as to correct any abnormalities. This study was designed to report about the various variations of the lung sizes and long term effect of COVID 19 on lungs and heart which would help for prevention of any health hazards in future And will also be strictly only used for the well-being of community, in publications and paper presentations.

I have been explained that radiological investigations will be conducted to evaluate my health status and for this purpose I fully agree.

I also agree to give all relevant information needed, in full and to the best of my knowledge to the researcher. It is clarified to me that no incentive, financial assistance or reimbursement will be provided to me for participating in the study whereas I do have the right to withdraw from the study at any time.

I am advised to contact **Dr. Madiha Mushtaque**

Mobile number: **03342647823** or visit **PNS Shifa** hospital in case of query.

Name of Participant: _____

S/o, D/o, W/o_____

Signature of Participant: _____

Name of Researcher: _____

Signature of Researcher: _____

Date: _____

مریض کی تحریری باخبر رضامندی فارم

میں رضاکارانہ طور پر اور اپنی مرضی سے تحقیقی منصوبے میں شرکت کی رضامندی دے رہا ہوں جس کا مقصد کوویڈ 19 نمونیا کے بعد پھیپھڑوں میں شکلی تغیرات کا مقصد ہے۔ یہ منصوبہ ان تبدیلیوں کا جائزہ لے گا جو مستقبل میں کوویڈ ۱۹ کی روک تھام اور علاج کے طریقہ کار میں مدد گار ہوں گی۔

مجھے اس منصوبے میں حصہ لینے کی نوعیت اور اہمیت کی تفصیل سے وضاحت کی گئی ہے کہ پھیپھڑوں اور دل کی غیر معمولی صورتحال اور سائز کا تجزیہ کرنے سے مجھے کوویڈ 19 کے علاج کے منصوبے پر عمل کرنے میں مدد ملے گی۔ فائبروسس اور پھیپھڑوں کے سائز میں تبدیلیوں کی صورت میں یہ ڈسپنیا اور کھانسی کا سبب بن سکتا ہے۔ میں فراہم کردہ وضاحت کو سمجھتا ہوں۔

مجھے بتایا گیا ہے کہ تمام نتائج اور میرے ذاتی ڈیٹا کو سختی سے خفیہ رکھا جائے گا اور اسے صرف پلمونالوجسٹ کے فائدے کے لئے استعمال کیا جائے گا تاکہ علاج کا منصوبہ بنایا جاسکے تاکہ کسی بھی غیر معمولی صورتحال کو دور کیا جاسکے۔ یہ مطالعہ پھیپھڑوں کے سائز کے مختلف تغیرات اور پھیپھڑوں اور دل پر کوویڈ 19 کے طویل مدتی اثرات کے بارے میں رپورٹ کرنے کے لئے ڈیزائن کیا گیا تھا جو مستقبل میں صحت کے کسی بھی خطرات کی روک تھام میں مدد کرے گا اور اشاعتوں اور کاغذی پیشکشوں میں صرف کمیونٹی کی فلاح و بہبود کے لئے بھی سختی سے استعمال کیا جائے گا۔

مجھے وضاحت کی گئی ہے کہ میری صحت کی حیثیت کا جائزہ لینے کے لئے ریڈیولوجیکل تحقیقات کی جائیں گی اور اس مقصد کے لئے میں اس سے مکمل طور پر اتفاق کرتا ہوں۔

میں تمام متعلقہ معلومات، مکمل طور پر اور اپنی معلومات کے مطابق محقق کو دینے پر بھی اتفاق کرتا ہوں۔ مجھے واضح کیا گیا ہے کہ مجھے مطالعے میں حصہ لینے کے لئے کوئی ترغیب، مالی امداد یا معاوضہ فراہم نہیں کیا جائے گا جبکہ مجھے کسی بھی وقت مطالعے سے دستبردار ہونے کا حق حاصل ہے۔

مجھے مشورہ دیا گیا ہے کہ **ڈاکٹر مدیحہ مشتاق**سے رابطہ کریں
موبائل نمبر: پوچھ نے کی صورت میں **پی این ایس شفا**اسپتال **03342647823**یا وزٹ کریں۔
شرکا کا نام: ___
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محقق کا نام: ___
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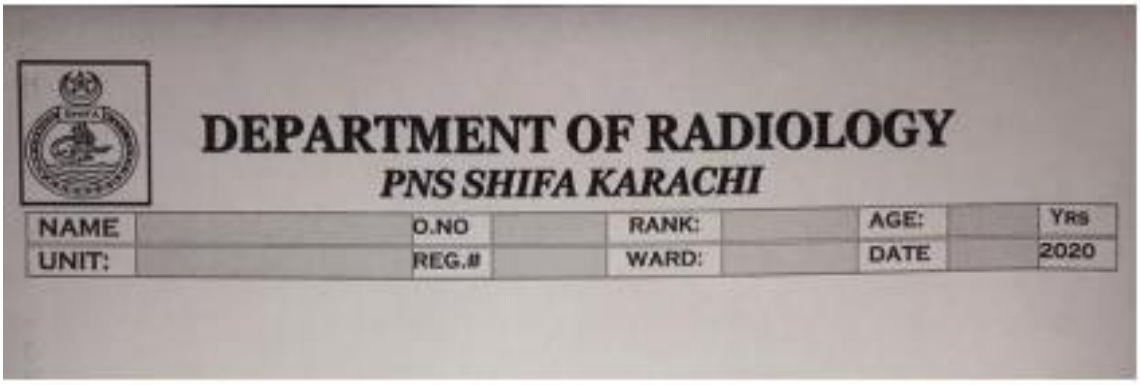
(D) Questionnaire

1.	DEMOGRAPHIC DETAILS	
2.	NAME	
3.	AGE	
4.	ADRESS CONTACT NUMBER	
5.	GENDER	
6.	PRESENTING COMPLAIN	
7.	PAST MEDICAL HISTORY	
8.	COMORBITIES	
9.	LENGTH OF HOSPITAL STAY DUE TO COVID 19 PNEUMONIA	
10.	OXYGEN SATURATION ON ADMISSION	
11.	RECEIVED STEROID	
12.	HIGH FLOW OXYGEN	

CT SCAN VIEW

- Coronal plane
- Axial View
- Sagittal view
- Fibrosis
- Coronal, axial, and sagittal diameter of right and left lung
- Transverse and longitudinal diameter of heart

(E) Hospital / Institute Card



DEPARTMENT OF RADIOLOGY
PNS SHIFA KARACHI

NAME		O.NO		RANK:		AGE:	YRS
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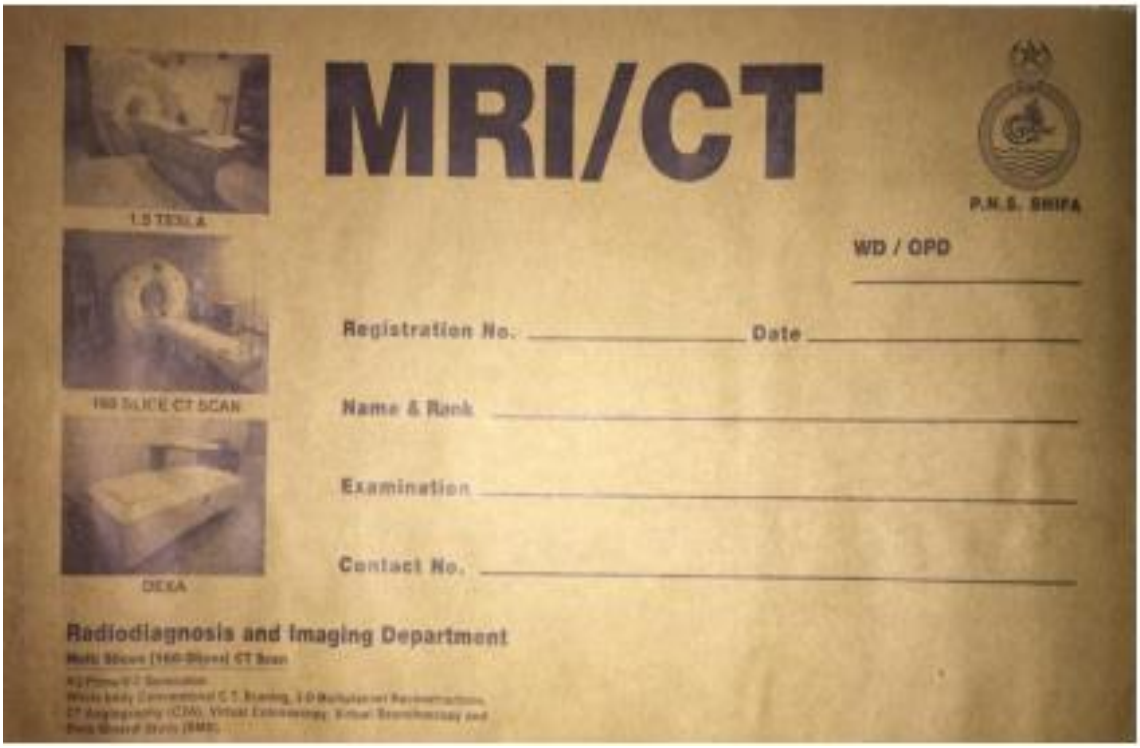

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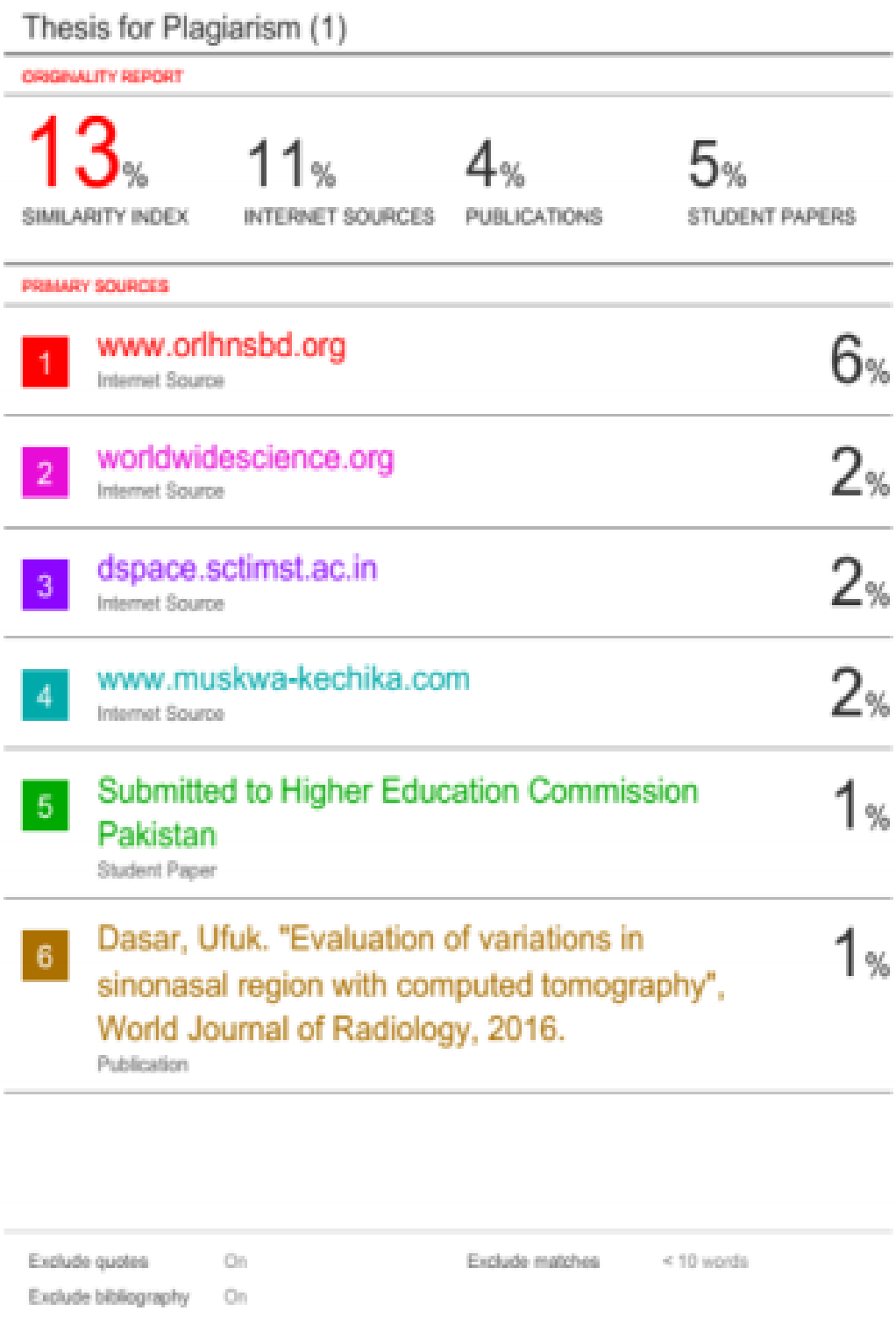

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