# Assessment of the Post-Pandemic Renal and Thyroid Health of Sars-CoV-2 Exposed Individuals in Ibadan, Nigeria

**Temitope David OGUNLEYE**
**LCU/PG/001442**

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## Certification

This is to certify that **Temitope David Ogunleye** with the Matric number **LCU/PG/001442,** carried out this research work titled "Assessment 0f The Post-Pandemic Renal and Thyroid Health of Sars-CoV-2 Exposed Individuals in Ibadan, Nigeria" in the Department of Biological Sciences, Faculty of Natural and Applied Sciences**,** Lead City University, Ibadan, Oyo State, for the award of PhD in Biology (Immunology) and this has not been previously submitted.

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**Dr, Azuka Patrick Okwuraiwe** **Date**

(Supervisor)

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**Dr. Felicia Adesina** **Date**

(Head of Department)



## Dedication

This research is dedicated to God, and to my lovely family.

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**Abstract**

This study assessed the post-pandemic renal and thyroid health of SARS-CoV-2-exposed individuals in Ibadan, Nigeria. Corona Virus Disease of 2019 (COVID-19) infection is caused by a novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The main manifestation is an acute respiratory illness with interstitial and alveolar pneumonia; however, the possibility of the virus invading other organs cannot be disregarded. Organs, such as the kidney and thyroid glands have been discovered to express the SARS-CoV-2 receptor known as the angiotensin-converting enzyme 2 (ACE2), implying that they are target tissues. Presently, information is scarce on the impact of SARS-CoV-2 viral infection on renal and thyroid functions after the pandemic. Hence this study provides data for the post-pandemic thyroid and renal status of SARS-CoV-2 exposed individuals. This is a cross-sectional study, involving random venous blood samples collection from subjects at different local governments in Ibadan, Oyo state. The socio-demographic information was obtained from 165 subjects comprising 85 unexposed samples; those who tested negative for SARS-CoV-2 virus, who also tested negative for SARS-CoV-2 antibody, and 80 exposed who tested positive for SARS-CoV-2 virus and equally tested positive to SARS-CoV-2 antibody. Inflammatory marker (CRP), renal markers (Cystatin C, Urea, Creatinine, electrolytes; $Na^+$, $K^+$, $Cl^-$, $HCO_3^-$), and markers of thyroid function (FT3, FT4, TSH) of the two groups were compared using independent sample T-test. There were no significant differences ($p > 0.05$) in the Mean ± SD of the inflammatory marker, renal markers, and thyroid function markers of the unexposed samples and exposed samples. This suggests that individuals exposed to SARS-CoV-2 during the pandemic fully recovered. Further studies should be done to determine the post-pandemic effects of viral infection on other vital organs that express the SARS-CoV-2 receptor.

**Keywords**: SARS-CoV-2, Cystatin C,
**Word Count:** 293

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## List of Acronyms

| Abbreviation | Meaning |
|---|---|
| ACE -2 | Angiotensin Converting Enzymes 2 |
| AKI | Acute Kidney Injury |
| ARDS | Acute Respiratory Distress Syndrome |
| CD | Clusters of Differentiation |
| CKD | Chronic Kidney Disease |
| COVID-19 | Coronavirus Disease 19 |
| CysC | Cystatin C |
| ESRD | End Stage Renal Disease |
| FT3 | Free- Tri-iodothyronine |
| FT4 | Free-Thyroxine |
| HBA1C | Glycosylated Haemoglobin |
| IL | Interleukin |
| MCP-1 | Monocyte Chemo-attractant Protein-1 |
| MERS | Middle East Respiratory Disease |
| RNA | Ribonucleic Acid |
| RT-PCR | Real-time Reverse Transcription Polymerase Chain Reaction |
| SARS-CoV-2 | Severe Acute Respiratory Syndrome Coronavirus-2 |
| TMPRSS2 | Transmembrane Protease Serine 2 |
| TNF | Tumor Necrosis Factor |
| TSH | Thyroid Stimulating Hormone |
| WHO | World Health Organization |

# Chapter One

# Introduction

## 1.1 Background to the Study

An unusual acute respiratory illness outbreak started in Wuhan, China, in December 2019. This quickly expanded outside of Wuhan. It was conclusively established that a novel coronavirus was to blame given its significant homology (80%) to SARS-CoV, which caused acute respiratory distress syndrome (ARDS) and high mortality between 2002 and 2003. The novel coronavirus was given the name severe acute respiratory syndrome coronavirus-2 (SARS–CoV–2, 2019–nCoV)[1]. The outbreak of SARS-CoV-2 was assumed to have first started via a zoonotic transmission comparable to SARS and Middle East Respiratory Disease (MERS), related to the seafood market in Wuhan, China. Subsequently, it was realized that human-to-human transmission was a significant factor in the outbreak that followed[2]. The World Health Organization declared a pandemic and named the illness brought on by this virus Coronavirus Disease 19 (COVID-19). As has been reported in the year 2020, in about 200 countries and territories, COVID-19 has had a significant influence on a lot of individuals throughout the world[3]. As of March 11, 2023, around 681,419,103 confirmed cases and 6,811,353 deaths worldwide have been reported because of the coronavirus COVID-19[4].

COVID-19 became a global pandemic on the 11th of March 2020, as announced by the World Health Organization. However, on the 27th of February 2020, the first case of the virus was reported in Lagos State, Nigeria by the Federal Ministry of Health[5]. Nigeria became the third country in Africa after Egypt and Algeria to recognize an imported COVID-19 case when the Federal Ministry of Health announced on February 27, 2020, the first COVID-19 case in Ogun State. The index case involved an Italian national who, on February 24, 2020, took a flight from

Milan, Italy, to Lagos, Nigeria, and then drove the same day to his company's location in Ogun State. He presented with symptoms that were consistent with COVID-19 on February 26, 2020, at his firm's clinic. He was then sent to the Infectious Disease Hospital (IDH) in Lagos, where, on February 27, 2020, real-time reverse transcription polymerase chain reaction (RT-PCR) was utilized to confirm the diagnosis of COVID-19[5].

Though some organ systems are also affected, the respiratory system is where the SARS-CoV-2 virus primarily manifests itself. The original case series from Wuhan, China, described symptoms associated with lower respiratory tract infections, such as fever, dry cough, and dyspnea. Other symptoms included a headache, vertigo, widespread weakness, nausea, and diarrhea[6]. This condition may also be lethal; there have been more and more deaths worldwide from patients with severe illnesses. According to epidemiological studies, mortality rates are higher in the aging population and much lower in children[6]. As the outbreak went on, the number of cases among people 65 years of age and older went up even more. There were also signs that the number of infections among young children (under 18) was going up. Even though there were more men affected at first, there was no clear difference between the sexes as the number of cases grew[7]. The average time of incubation was 5.2 days. 2.3% of all cases resulted in fatalities. Using information from two hospitals in Wuhan, the risk factors for in-hospital death were investigated[7]. The multi-variable analysis revealed that older age, a higher sequential organ failure assessment (SOFA) score, and d-dimer >1 g/mL on admission were risk factors. The existence of coronary artery disease, diabetes, and hypertension was also regarded as a risk factor in the univariable analysis. Most patients died from multi-organ failure, according to a research study of 85 fatal COVID-19 patients in Wuhan with a median age of 65 years, as respiratory failure, shock, and ARDS were present in 94%, 81%, and 74% of cases, respectively[8].

Coronaviruses are positive-sense, single-stranded, enclosed RNA viruses that are about 30 kb in size. A wide range of host species are infected by them [9]. Based on their genetic structure, they are classified into four genera, with only mammals being infected by α and β coronaviruses [10]. Human coronaviruses, including 229E and NL63, which are both members of the alpha group of coronaviruses, can cause the common cold and croup. In contrast, SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV), and SARS-CoV-2 are assigned to the beta group of coronaviruses [9].

Five stages make up the virus's life cycle within the host: attachment, penetration, biosynthesis, maturation and release. The virus adheres to host receptors; after this attachment, the virus enters the host cells through endocytosis or membrane fusion after attaching to host receptors (penetration). The viral RNA enters the nucleus of the host cells once the viral components have been released inside and the viral proteins are produced using viral mRNA (biosynthesis). Then, after maturing, additional virus particles are produced and discharged, which are then made up of four structural proteins: spike (S), membrane (M), envelop (E), and nucleocapsid (N)[11]. The spike protein is a transmembrane trimetric glycoprotein that projects out from the surface of the virus. It controls host tropism and is responsible for coronavirus variability. The spike is made up of two functional subunits: the S1 subunit which binds to the host cell receptor and the S2 subunit fuses the viral and cellular membranes [12]. The coronavirus's spike proteins bind to renin-angiotensin-aldosterone system (RAAS) regulators called angiotensin-converting enzyme 2 (ACE2) receptors on the epithelial surface of human cells. A serine protease called TMPRSS2 is recruited by SARS-CoV-2 to aid in viral protein priming and cytoplasmic entry[13]. The expression of SARS-CoV-2 cell receptor (ACE2 receptor) genes varies among human organs, with the small intestine having the highest levels of expression, followed by the hypothalamus, pituitary, testes, heart, thyroid, kidney, and lungs at a varying levels[14]. After SARS-CoV-2 binds

to the host protein, a protease cleaves the spike protein. Afterwards a two-step sequential protease cleavage to prime the SARS-CoV and MERS-CoV spike proteins and cleave the spike protein to activate it at the S′2 location, which is close to a fusion peptide in the S2 subunit. The S1 and S2 subunits are still non-covalently attached after the S1/S2 cleavage site and the distal S1 subunit helps keep the membrane-anchored S2 subunit stable in the prefusion condition [15]. The spike is apparently activated for membrane fusion by further cleavage at the S′2 location via irreversible conformational changes. The coronavirus spike is distinct from other viruses in that it can be cleaved and activated by a variety of proteases. The presence of a furin cleavage site ("RPPA" sequence) at the S1/S2 site is one of the traits that set SARS-CoV-2 apart from other coronaviruses. In stark contrast to the SARS-CoV spike, which was integrated into assembly without cleavage, the S1/S2 site of SARS-CoV-2 was completely susceptible to cleavage during biosynthesis[16]. The widespread expression of furin likely renders this virus particularly dangerous even if the S1/S2 site was also exposed to cleavage by other proteases such as transmembrane protease serine 2 (TMPRSS2) and cathepsin L[16].

The majority of reports from immunological research involving patients with severe COVID-19 show that lymphopenia was present in patients, particularly when there was a decrease in peripheral blood T cells. Increased plasma levels of proinflammatory cytokines, such as interleukin (IL)-6, IL-10, granulocyte-colony stimulating factor (G-CSF), monocyte chemoattractant protein 1 (MCP1), macrophage inflammatory protein (MIP)-1, and tumor necrosis factor (TNF)—have been observed in patients with severe diseases[17]. Patients' IL-6 levels increased with the severity of their diseases. An increase in the expression of CD69, CD38, and CD44 in these patients revealed that CD4+ and CD8+ T cells had been activated, while a higher proportion of checkpoint receptor Tm3+PD-1+ subsets in CD4+ and CD8+ T cells indicated that T cells were similarly worn down. In CD8+ T cells, levels of NK group 2-member

A (NKG2A), another indicator of exhaustion, were increased[18]. IL-8, a chemoattractant for neutrophils and T cells are produced with IL-6 by virus-infected lung epithelial cells.

The metalloproteinase angiotensin-converting enzyme 2 (ACE2) is a carboxy-terminal dipeptidyl peptidase. The main physiological function of ACE2 is to control blood pressure and vasoconstriction. The coronavirus spike (S) protein could be cleaved by transmembrane protease serine type 2 (TMPRSS2), a member of the type II transmembrane serine protease family [14]. The entry of SARS-CoV and SARS-CoV-2 into the host cells was shown to depend on ACE2 and TMPRSS2. SARS-CoV-2 cell entry is dependent on the S protein's affinity for a particular cellular receptor and the priming of the S protein by host cell proteases. The pathway of SARS-CoV-2 infection and the infected organ may depend on the expression and distribution of ACE2 and TMPRSS2, since receptors and mediators of virus entry are crucial for identifying the viral host and organ. According to studies, ACE2 and TMPRSS2 are expressed in extrapulmonary organs such as the heart, kidney, liver, colon, esophagus, brain, gallbladder, and testis in addition to lung tissues[14]. This suggests that SARS-CoV-2 may also impact extrapulmonary organs.

Expression analyses from the Common Fund's Genotype-Tissue Expression (GTEx) Program show that ACE2 is expressed the fifth most in the kidney[19]. The public single-cell transcriptome dataset of healthy volunteers' normal kidneys was analyzed to investigate the expression of ACE2 in the kidney, and the findings revealed that ACE2 was distributed throughout a variety of cell types but was primarily enriched in proximal tubule cells[19]. In contrast to immune cells and glomerular parietal epithelial cells. It was also verified by the unique ACE2 expression in tubular cells from the Gene Expression Omnibus (GEO) dataset. The Cancer Cell Line Encyclopedia (CCLE), GTEx database, and Human Protein Atlas dataset were used to gather RNA and protein expression data of ACE2 in various human tissues and cancer cell lines [19]. The findings showed

that both mRNA and protein expression levels of ACE2 were relatively high in kidney cells, particularly in renal tubular cells. Meanwhile, a study report analyzed the data of kidney tissues in scRNA-Seq datasets and discovered that either proximal tubular cells or tubular progenitor cells in the kidney co-expressed ACE2 and TMPRSS2[20]. The scRNA-seq data from the GEO dataset (GSE 134355) revealed that ACE2 and TMPRSS2 expression levels were high in nephron epithelial cells, epithelial cells, endothelial cells, and mesangial cells of the kidney. And recently, it was discovered that the TMPRSS2 gene and ACE2 were co-expressed in kidney podocytes [21, 22].

The kidney has been identified as a significant target organ for SARS-CoV-2 infection due to the presence of ACE2 receptors, and laboratory tests have shown that certain COVID-19 patients' urine samples have tested positive for the virus [23]. One of the most serious complications of COVID-19 is acute kidney injury because SARS-CoV-2 can infect renal intrinsic cells like proximal tubular epithelial cells and cause renal dysfunction. The incidence of acute kidney injury as a consequence of COVID-19 was 7% in 41 cases published in the Lancet, and all of them progressed to severe instances [24]. Acute kidney injury occurred in 0.5% of the 1099 COVID-19 patients, and the severity rate was 83.3% [25]. Renal failure, defined as an increase in serum creatine, blood urea nitrogen, the development of proteinuria, or the presence of hematuria, was associated with a considerably greater mortality risk than normal renal function in a subsequent cohort analysis included 701 COVID-19 participants [26]. Renal impairment was a standalone risk factor for mortality in hospitalized patients. These investigations showed that one of the most serious consequences that affected COVID-19 patients was acute kidney damage. The kidneys are high in ACE2. Even more than in the heart, the renal cortex exhibits strong ACE2 activity [25]. The expression level of ACE2 reduced in both the acute kidney injury model and multiple models of chronic kidney disease brought on by hypertension, diabetes, and

nephrectomy, which altered the homeostasis of RAS in the kidneys and exacerbated the pathological alterations in the kidneys. As discussed, mounting evidence has also shown that ACE2 was essential for the pathophysiology and development of renal disorders. ACE2 deletion may exacerbate fibrotic pathologies in obstructive renal disorders and renal dysfunction models in ischemia/reperfusion[25]. More research is needed to determine how ACE2 may have contributed to the renal dysfunction seen by COVID-19 individuals as well as the clinical outcomes in COVID-19 patients who also had chronic kidney disease. Another significant discovery was that patients with more severe clinical manifestations of COVID-19 had greater serum concentrations of pro-inflammatory mediators and immune cells malfunction, which exacerbated cytokine storm and resulted in kidney failure, as seen in sepsis disease[27].

The fact that virus-like particles can be found in the follicular epithelium of patients with subacute thyroiditis (SAT) and, more recently, in some independent case reports of SAT linked to SARS-CoV-2 shows that SARS-CoV-2 could also infect thyroid cells[28]. The thyroid's anatomical proximity to the upper airways, a major route for coronavirus entry, lends support to the notion that the thyroid might be a target of SARS-CoV-2. In fact, it has been previously observed that a significant proportion of people with severe acute respiratory syndrome (SARS-CoV) exhibit abnormalities in thyroid function and disturbances of the follicular architecture. Clinically, the fact that some COVID-19 patients experience ear pain, which is a typical SAT symptom, would support the idea that SARS-CoV-2 could infect the thyroid and cause subacute inflammation[29]. Due to the possibility that SAT-related thyrotoxicosis may be a factor in the cardiovascular problems seen in COVID-19 patients, this pathologic process may eventually be clinically significant. After examining two separate databases, it was evidenced that ACE-2 is present in various human organs, including the thyroid[30]. Though direct evidence for the presence of the ACE-2 mRNA in thyroid cells is still absent.

Thyroid and kidney functions can interact in several ways when one or both organs are in pathological states. Thyroid hormones have an impact on renal development and physiology. The glomerular filtration rate and renal blood flow are both increased by the pre-renal and intrinsic renal actions of thyroid hormones (GFR)[31]. Reduced GFR is a sign of hypothyroidism, and increased GFR and enhanced renin-angiotensin-aldosterone activation are signs of hyperthyroidism. Low triiodothyronine (T3) syndrome, a feature of chronic kidney disease (CKD), is now recognized as a component of an atypical nonthyroidal condition. Primary hypothyroidism and subclinical hypothyroidism are more common in CKD patients. The physiological advantages of a hypothyroid state in CKD and the danger of hyperthyroidism accelerating the disease highlight the need for a cautious approach to treating thyroid hormone abnormalities in CKD[31].

Early in the COVID-19 pandemic, pulmonary symptoms were the focus of clinical practice and research. However, there are growing evidence suggesting both direct effects on several organ systems as well as indirect effects on other organ systems and disease processes, like cancer, renal, endocrine, and cardiovascular illnesses, due to changes in patient behaviors and healthcare delivery[32]. Patients with COVID-19 and other underlying diseases may experience a spectrum of symptoms and organ failure due to the widespread expression of the ACE2 receptor and its variable density. Infection with other coronaviruses, such as severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS), has been linked to multiorgan damage and long-term clinical outcomes[33]. Due to the high number of COVID-19 patients admitted to intensive care units (ICUs), long-term effects of COVID-19 may parallel those seen in post intensive care syndrome or post sepsis syndrome[33].

SARS-CoV-2 viral infection continues to impact the world greatly, especially with the emergence of Delta, Omicron, and other variants in various clinical studies[34, 35]. Acute Kidney Injury has been reported as a critical non-respiratory clinical manifestation of COVID-19 regardless of any prior kidney damage [36, 37, 38]. Aberrant thyroid function has also been noted in the weeks following the SARS-CoV-2 infection [39]. Through retrospective observational studies and case reports, many thyroid conditions, including non-thyroidal sickness syndrome (NTIS), subacute thyroiditis (SAT), thyrotoxicosis, and hypothyroidism, have been identified in individuals post-COVID-19 infection [39, 40]. These studies raise the question of whether or not thyroid function should be given extra attention in COVID-19 patients, even if a cause-and-effect relationship between the infection and the start of thyroid dysfunction has not yet been proven from a mechanistic point of view. Presently, there is scarce and conflicting information on the direct impact of the viral infection on kidney and thyroid function and its impact on these organs' health.

A lot of effort is being expended to combat the pandemic. Several research are ongoing into development of therapies and vaccines are being rolled out against the pandemic. Patients diagnosed and hospitalized due to SARS-CoV-2 viral infection are reported to have significant risk of developing AKI and thyroid dysfunction. This can lead to infection severity and a high mortality rate. This exact effect is unclear and there is a need for consistent monitoring of renal and thyroid function during and after infection. This is because individuals who had AKI have a high risk of developing chronic kidney disease. Evidence of abnormal thyroid function has been seen after the phase of convalescence following COVID condition. The "cytokine storm" may be a key mediator in this situation, even though the cellular and molecular mechanisms are not fully understood. Future research is therefore required to more thoroughly explore the molecular and

clinical basis of thyroid dysfunction brought on by COVID-19 for proper management of patients.

There is a paucity of information on the prevalence of thyroid disorders in Nigeria, but a study in southeastern Nigeria reveals a prevalence of 2.4%, which is greater than the 1.6% rate observed for Southwestern Nigeria. The increasing incidence of thyroid dysfunction in Nigeria necessitates the need to ascertain thyroid function among individuals within-risk factors, for which COVID-19 has been identified[41].

According to the most recent survey, AKI causes about 2 million deaths annually, and those who survive have a higher risk of developing chronic renal disease. An early identification and treatment of AKI could successfully stop the outcome from happening [42] . Despite significant advancements in the histology and etiology of AKI, there was still debate regarding clinical detection and diagnosis[43]. Today, AKIN (acute kidney injury network) and RIFLE (risk, injury, failure, loss) and ESRD both advocated that the increase in serum creatinine or reduction in urine output should be utilized as the most generally applied and widely accepted clinical standard for the definition and diagnosis of AKI[44]. Unfortunately, serum creatinine was unable to accurately reflect the timing and type of renal injury because of its poor sensitivity and specificity, as well as the 48 h-72 h time requirements [45] . However, additional parameters like age and acute and chronic renal insufficiency had an impact on serum creatinine. These investigations revealed that the need for more precise and effective diagnostic tools for AKI was essential. Early diagnosis of acute kidney injury (AKI) is currently a challenging task because the commonest method of estimating urea and creatinine in diagnosing AKI may cause a delay in early recognition of AKI due to its limitations [46] . Some of the limitations include Insensitivity to little changes in glomerular filtration rate (GFR), Creatinine is also a late marker of altered GFR, non-specificity

to disease process and it is affected by some clinical attributes (age, weight, gender, volume status, medication use)[47].

An important concern for patients receiving critical care is acute kidney damage (AKI; also known as acute renal failure), with sepsis being the most frequent cause of AKI in the intensive care unit[48]. The death rates for septic AKI have remained high due to the lack of sensitive and precise biomarkers for identifying renal cell injury. Neutrophil gelatinase-associated lipocalin (NGAL), a recent discovery using genomic, transcriptomic, and proteomic methods, is now recognized as an early indicator of AKI[48]. In a variety of clinical contexts, including contrast-induced nephropathy, AKI following heart surgery or kidney transplantation, and AKI in the critical care setting, NGAL has been studied. Similar to troponin for acute myocardial infarction, NGAL is a promising biomarker for AKI with an overall sensitivity of 0.815 (95% confidence interval, 0.732-0.892)[48].

The CST3 gene encodes Cystatin C (CysC), a cysteine protease inhibitor that is a member of the type 2 cystatin gene family. Cystatins play an important physiological role in controlling the activity of endogenous proteinases, which are frequently released or leaked from the lysosomes of sick or dying cells. The entire amino acid sequence of CysC was established in 1981 after it was initially identified in cerebrospinal fluid in 1961. It has a molecular mass of 13,343 Da, 120 amino acids, and is non-glycosylated. All cystatins share a conserved glycine at position 11 at the N-terminus, which is found in CysC. For both binding affinity and inhibition specificity, the N-terminal region of cystatin is crucial. Human CysC's N-terminal 10 peptide truncation diminishes cathepsin B and cathepsin H inhibition by more than 1,000- and 50-fold, respectively. CysC is continuously produced by all nucleated cells, and it is freely filtered in the renal glomeruli without being reabsorbed[49]. The primary catabolic location of CysC in the kidney is the proximal tubular cells. Glomerular ultrafiltration virtually entirely removes the protein from

the blood circulation. CysC is hardly detectable in urine under normal circumstances, but it becomes more prevalent when proximal tubular cells are damaged. In mildly impaired renal function, free filtration may allow CysC to more accurately reflect renal function than serum creatinine. Some studies have also demonstrated that using CysC-based equations for calculating GFR is more accurate than using creatinine-based calculations [50] . Also, compared to serum creatinine, CysC is less affected by muscle mass and caloric intake. Corticosteroids, which are frequently prescribed to people who have had a kidney transplant, are among the medications that have been identified as having an impact on CysC production. These qualities among others make Serum levels of cystatin C a more precise test of kidney function (as represented by the glomerular filtration rate, GFR) than serum creatinine levels[51].

One of the co-morbidities implicated in the severity of SARS CoV-2 viral infection is diabetes. Glycosylated hemoglobin is essential in its diagnosis. Almost 40 years ago, glycated hemoglobin (HbA1c) was initially recognized as an "unusual" hemoglobin in diabetic individuals. HbA1c shows the average glucose level in plasma during the past eight to twelve weeks [52] . It can be conducted at any time of day and requires no additional preparations, such as fasting. These characteristics have made it the recommended method for measuring glycemic control in diabetics [52] . There is emerging evidence that diabetes is closely associated with an increased chance of contracting COVID-19 and with bad outcomes. However, the influence of the severity of COVID-19 on glycemic indices remains unknown. According to the study, severe COVID-19 infection was substantially related with elevated blood glucose levels. As viral infection and hyperglycemia interact negatively, our study emphasizes the necessity to effectively manage blood glucose in COVID-19-infected patients to enhance their prognosis [53] . Diabetes mellitus (DM) is the major cause of chronic kidney disease and needs to monitored. As it accounts for roughly 45 percent of all instances of end-stage renal disease (ESRD) in dialysis patients. Time-

averaged mean levels of glycemia, as measured by glycosylated hemoglobin (HbA1C) level, are the gold standard for regulating glycemia and reducing the problems associated with diabetes in post-acute phase of COVID-19[54].

Furthermore, one of the most typical endocrine conditions found worldwide is thyroid disease. Enlargement of the thyroid gland, symptoms of decreased or increased hormone production, or complications from the disease itself might all be present[55]. Due to the multiple functions of thyroid hormones (THs), which include controlling the basal metabolic rate, which is necessary for normal growth, mental development, and sexual maturation, as well as increasing the sensitivity of the cardiovascular and central nervous systems to catecholamines, cardiac output and heart rate, a diagnostic challenge may arise both clinically and biochemically[55]. A clinical impression that suggests thyroid malfunction or overt symptoms and indications that are indicative of hyperthyroidism or hypothyroidism may serve as the basis for a request for thyroid function tests (TFTs). TFT can be used for thyroid disease screening, diagnosis, monitoring, and treatment evaluation. Thyroid-stimulating hormone (TSH), total triiodothyronine (TT3) and/or free triiodothyronine (FT3), and total thyroxine and/or free thyroxine (FT4) are the analytes that are frequently analyzed in TFT[56]. The fourth generation of TSH assays has helped to increase the diagnostic sensitivity and specificity of the TH assay over time. Many professional organizations, including the American Thyroid Association, the National Academy of Clinical Biochemistry, and the Royal College of Physicians in London, have released a variety of guidelines on the use of laboratory research of thyroid problems[57]. TSH has been emphasized as the initial screening test for thyroid disorders. Thyroxine and triiodothyronine secretion, which have a log-linear negative feedback effect on pituitary thyrotrophs, are controlled by pituitary TSH secretion. TSH is the best indication of subtle changes in thyroid function because of this connection, which causes modest changes in the

concentration of free TH to result in substantial changes in the serum concentration of TSH [57] . The thyroid gland's main hormone to be secreted is T4. The peripheral conversion of T4 through 5'-mono-deiodination in diverse tissues accounts for around 80% of the serum T3 concentration. Just 0.02% of T4 and 0.2% of T3 circulate in the bloodstream free; the majority of THs are linked to plasma proteins. In comparison to overall hormone levels, FT4 and FT3 levels are more important [58]. The hormone's biologically active form is known as the free hormone. In addition, regardless of thyroid function, different inherited or acquired alterations in transporter proteins affect T4 and TT3 serum levels. Thyroid parenchyma has many ACE2 receptors, making it susceptible to SARS-CoV-2, the ACE2 was positively correlated with 3,5,3′-triiodothyronine (T3) and thyroxine (T4), suggesting it may be a valuable diagnostic for peripheral thyroid hormone activity [58] . The thyroid gland and viral infection interact via thyroid hormones and immunomodulatory signaling molecules. Viruses and immunological reactions may affect thyroid function. Thyroid hormones regulate various organ systems, including the circulatory and respiratory systems, which may affect COVID-19 progression[59]. Thyroid abnormalities have been associated to diabetes, obesity, kidney dysfunction, and liver illness, which increase the risk of COVID-19, therefore an uncontrolled thyroid disorder may worsen patient condition[59].



## 1.2 Statement of the Problem

The spread of the COVID-19 pandemic and the subsequent rise in its genetic variety have created an unusual scenario for the world. This virus's pathogenicity and ability to spread has increased due to the diversity in its genome. The possibility of SARS-CoV-2 impacting negatively on vital organs such as the kidney and thyroid is a major health concern.

Mortality rate of patients with severe acute kidney injury requiring dialysis has not decreased significantly over the last 50 years despite advances in supportive care[60].

With the report of SARS-CoV-2 causing renal dysfunction and the attendant economic and health complications then this must be critically studied[61].

Research suggests that patients who recover from COVID-19 may also experience post-acute sequelae, sometimes known as "long COVID," which can include symptoms in the kidneys, thyroid, and other extrapulmonary organ systems, in addition to the acute sickness. Regardless of any antecedent kidney impairment, acute kidney injury has been documented as a major non-respiratory clinical presentation in COVID-19[62]. According to several case studies, COVID-19 suffers from acute renal damage at varying rates[63].

Recent report has also described the onset of thyroid dysfunction in patients diagnosed with COVID-19 although such information is scarce in our environment[64]. Up till now, the incidence of organ dysfunction has been rising in Nigeria and around the world with noted interactions between thyroid and renal functions[65, 66, 67, 68].

It is important to note that diagnosis of acute kidney injury (AKI) is currently a challenging task because the commonest method of estimating urea and creatinine in diagnosing AKI may cause delay in early recognition of AKI[69]. In addition, there is scarcity of information on the effect of SAS-CoV-2 infection on renal and thyroid function.

### 1.3 Justification of the Study

A lot of effort is being expended to combat the pandemic; several researches are ongoing into development of therapies against SARS-CoV-2 infection. Patients diagnosed and hospitalized due to SARS-CoV-2 viral infection were reported to have significant risk of developing AKI and thyroid dysfunction. This can lead to infection severity and high mortality and pressure on the present health care system in Nigeria[70].

More so, it is unsure that those who were exposed to SARS-CoV infection during the pandemic are not having subclinical renal and thyroid dysfunctions which may progress to more severe health condition. Therefore, study on the effect of SARS-CoV-2 infection on renal and thyroid health of exposed individuals is very pertinent, for timely discovery, monitoring and management of post-pandemic clinical issues arising from SARS-CoV-2 infection.



## 1.4 Aim and Objectives of the Study

### Aim

The aim of this study is to determine the effects of post pandemic SARS-CoV-2 infection and on the renal, thyroid functions and markers of inflammation in individuals exposed to it.

The specific objectives of the study are to:

i. estimate the serum levels of SARS-CoV-2-antibody in both the exposed and unexposed groups.
ii. estimate the whole blood levels of glycosylated haemoglobin (HBA1C), in both the exposed and unexposed groups.
iii. estimate the serum level of cystatin c.
iv. estimate the serum level of electrolyte ($Na^+$, $K^+$, $Cl^-$, $HCO_3^-$), urea and creatinine.
v. estimate the serum level of C-reactive protein.
vi. estimate the serum level of free tri-iodothyronine (FT3).
vii. estimate the serum level of free thyroxine (FT4).

viii. estimate the serum level thyroid stimulating hormone (TSH).

## 1.5 Research Questions

i. What are the post-pandemic levels of markers of acute kidney injury (AKI) in the apparently healthy population who are not exposed to SARS-CoV-2 viral infection compared to population exposed to SARS-CoV-2 infection?

ii. Is AKI a post-pandemic frequent occurrence in individuals who tested positive for SARS-CoV-2 infection using RT-PCR method?

iii. What are the post-pandemic levels of markers of thyroid function in the apparently healthy population who are not exposed to SARS-CoV-2 viral infection compared to population exposed to SARS-CoV-2 infection?

iv. Is inflammation a post-pandemic frequent occurrence in individuals who tested positive for SARS-CoV-2 infection using RT-PCR method?

The exposed individuals are those who tested positive to the virus using RT-PCR method. The unexposed individuals are those who tested negative to the virus using RT-PCR method and are asymptomatic.

## 1.6 Significance of the Study

This study looked at the kidney and thyroid health of people in Ibadan who were exposed (infected) to SARS-CoV-2 during the pandemic. It will help find out what effect COVID-19 has on the thyroid and kidneys after recovery. This study gives a quantitative measure of thyroid and kidney function after COVID-19 and helps to find subclinical changes before the symptomatic phase. Hence, this study will show if/how important it is to routinely test thyroid and kidney function in the post-acute phase of COVID-19. It will also help inform clinicians on how to

properly advise patients with high-risk factors about this organs' dysfunction to reduce the associated damage involved. And help the government build the right capacity after the pandemic to cater properly for the populace, reducing mortality caused by COVID-19 in the post-acute phase. This will also help physicians and researchers recognize and monitor the range of symptoms, as well as set research goals, develop research priorities and therapeutic strategies for the affected organ systems (kidney and thyroid gland).

## 1.7 Scope of the Study

Whilst the immediate negative health problems related to the COVID-19 infection on the pulmonary system have been well documented, the impact of the virus on extra-pulmonary organs is poorly understood**.** The aim of this study is to assess the kidney and thyroid health of people in Ibadan who were exposed to SARS during the pandemic. The scope of the study is limited to recruiting a total of two hundred and seventy apparently healthy participants (males and females) in the age range of 18–60 years in different local government areas in Oyo State. They were recruited for the study after informed consent had been obtained from them. They were made up of an initial 120 SARS-CoV-2-exposed individuals and a matched cohort of 150 apparently healthy individuals without exposure to SARS-CoV-2 infection.

## 1.8 Limitations of the Study

This study involves recruitment of individuals who were exposed (tested positive to SARS-CoV-2 viral Infection). Difficulty in recruiting willing respondents therefore was a herculean task.

After contacting respondents who initially showed willingness to be part of the study, many easily declined sample collection due to fear of needle. Some respondents who initially agreed they were once exposed to SARS-CoV-2 viral infection, and agreed to be part of the survey, suddenly declined participation, claiming they were never exposed. Also, for the unexposed group, some participants who claimed they were never exposed and never symptomatic for the infection during the pandemic eventually ended up testing positive to the SARS-CoV-2 antibody.

Another difficulty encountered was during phlebotomy (blood sample collection) procedure. Some respondents without conspicuous veins had to be pricked more than once, and this caused them to be uncomfortable, some even withdrew from the study.



## 1.9 Operational Definition of Terms

**Reverse Transcription (RT)-PCR:** is used to amplify RNA targets. The enzyme reverse transcriptase turns the RNA template into complementary (c) DNA. Then, the cDNA is used as a template for PCR-based exponential amplification. RT-PCR can be carried out in a single step or two phases. The RT reaction and PCR reaction are combined in one tube during one-step RT-PCR. Primers must only be sequence-specific. The created cDNA is moved into a second tube for PCR during two-step RT-PCR. The oligo (dT), random hexamer, or gene-specific primers can be used. Although random primers can prime anything, including ribosomal RNA, oligo (dT) primers are typically favored because they hybridize to the 3' poly (A) tails in mRNAs (transcribed gene sequences)[71].

**Coronavirus Disease 2019 (COVID-19):** the respiratory condition that is the source of the continuing COVID-19 pandemic, is brought on by the severe acute respiratory syndrome

coronavirus 2 (SARS-CoV-2). The virus was once known as the human coronavirus 2019 and was given the preliminary name 2019 novel coronavirus (2019-nCoV) (HCoV-19 or hCoV-19)[72].

**The SARS-CoV-2 Spike Protein Antibody:** is a neutralizing antibody response to coronaviruses that is largely directed against the trimeric spike glycoprotein (S) on the viral membrane envelope. This protein acts as the mechanism for joining the membranes of the host cell and the virus. Three copies of the S1 subunit, which consists of the S1A through S1D domains and promotes attachment to target cells, are found in the coronavirus S proteins, as are three copies of the S2 subunit, which is responsible for facilitating membrane fusion. The receptor-binding domain is frequently the target of neutralizing antibody responses against SARS-CoV-2, SARS-CoV, and MERS-CoV S proteins (RBD; also called the S1B domain)[72].

**Chemiluminescence Immunoassay:** chemiluminescence (CL) is defined as the emission of electromagnetic radiation caused by a chemical reaction to produce light, while chemiluminescence immunoassay (CLIA) is an assay that combines chemiluminescence technique with immunochemical reactions. Like other labeled immunoassays (RIA, FIA, ELISA), CLIA utilizes chemical probes which could generate light emission through chemical reaction to label the antibody. In recent years, CLIA has gained increasing attention in different fields, including life science, clinical diagnosis, environmental monitoring, food safety and pharmaceutical analysis because of its high sensitivity, good specificity, wide range of applications, simple equipment, and wide linear range. This technique was used in the analysis of SARS-CoV-2 antibody, FT3, FT4and TSH[73].

**Thyroid Function Test:** is an organ function test used to assess the thyroid gland. The tests evaluate the blood's levels of triiodothyronine (T3), thyroxine (T4), and thyroid stimulating hormone (TSH). The pituitary gland in your brain produces and transmits TSH to the thyroid

gland. TSH regulates the synthesis of thyroid hormones (T3, T4), which are produced in response to TSH[56].

To quantify light absorption or the concentration of compounds in a solution, spectrophotometry is a common and affordable approach. Each substance in the solution either absorbs or transmits light of a particular wavelength when it is passed through the sample using a light beam. A spectrophotometer, which consists of two instruments, a spectrometer, and a photometer, is used to measure spectrometry. The photometer calculates the amount of light that goes through the sample after the spectrometer generates the light of the desired wavelength[74].

**Acute Kidney Diseases**: An abrupt decline in excretory kidney function is what is referred to as acute kidney injury (AKI). Acute kidney diseases and disorders (AKD), which include AKI, are a group of ailments characterized by a slight decline in kidney function or a persistent kidney dysfunction as well as an irreversible loss of kidney cells and nephrons that may progress to chronic kidney disease (CKD)[75].

**Chronic Kidney Disease:** Long-term, progressive decline in renal function is known as chronic kidney disease (CKD). Anorexia, nausea, vomiting, stomatitis, dysgeusia, nocturia, lassitude, weariness, pruritus, impaired mental acuity, muscle spasms and cramps, water retention, undernutrition, peripheral neuropathies, and seizures are among the symptoms that slowly worsen and progress to more severe phases. The ability of the kidneys to maintain fluid and electrolyte homeostasis is hampered by decreased renal function. Early falls in urine concentration are followed by declines in urine excretion of excess phosphate, acid, and potassium. Urine osmolality is often fixed at around 300 to 320 mOsm/kg, which is close to that of plasma (275 to 295 mOsm/kg), when renal failure is advanced (glomerular filtration rate

[GFR] 15 mL/min/1.73 m2) and urinary volume does not respond quickly to changes in water consumpti[76].

**Autoimmune Thyroid Disorders:** (AITD) are brought on by immune system dysregulation that results in an immunological attack on the thyroid. Organ-specific autoimmune diseases (AITD) are T cell-mediated. The most prevalent pathological abnormalities of the thyroid gland are autoimmune thyroid disorders (AITD). Graves' disease (GD) and Hashimoto's thyroiditis (HT), both of which are characterized by lymphocytic infiltration of the thyroid parenchyma, are the two primary clinical manifestations of the AITD[77].

A thyroid immune response known as subacute thyroiditis frequently follows an upper respiratory infection. Just above the middle of your collarbones, in the neck, is where the thyroid gland is situated. A self-limiting thyroid illness called subacute thyroiditis is characterized by a triphasic clinical course that includes hyperthyroidism, hypothyroidism, and a return to normal thyroid function. 10-15% of patients who arrive with thyrotoxicosis and 10% of those who present with hypothyroidism may both have subacute thyroiditis. The presence and stage of subacute thyroiditis can be detected through thyroid function testing[74].

## Endnotes


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# Chapter Two

# Literature Review

## 2. I Conceptual Review

Coronavirus Disease 2019 (COVID-19), the new millennium's pandemic, has caused unprecedented issues for global health. The causative agent is a new encapsulated RNA coronavirus 2 identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The People's Republic of China (PRC), a nation in East Asia, is where the pandemic started in the city of Wuhan. This quickly expanded outside of Wuhan [1]. Due to its high similarity (80%) to SARS-CoV, which caused acute respiratory distress syndrome (ARDS) and high mortality between 2002–2003, the novel coronavirus was given the name severe acute respiratory syndrome coronavirus-2 (SARS–CoV–2, 2019–nCoV)[2]. SARS-CoV-2 was thought to have first spread by a zoonotic transmission linked to a seafood market in Wuhan, China. Subsequently, it was realized that transmission from person to person was a significant factor in the outbreak that followed. Coronavirus disease 19 (COVID-19), the name of the illness brought on by this virus, was deemed a pandemic by the World Health Organization (WHO)[3]. A lot of people have been impacted by COVID-19, which has been recorded in about 200 nations and territories. Over 4,487,553 cases have been documented globally as of April 7th, 2020, according to the Center for Systems Science and Engineering (CSSE) at John Hopkins University[4].

Although other organ systems are also affected, the respiratory system is where SARS-CoV-2 virus primarily manifests itself [1]. The original case series from Wuhan, China, revealed symptoms associated with lower respiratory tract infections, such as fever, dry cough, and dyspnea. In addition, many reported experiencing headaches, vertigo, widespread weakness, vomiting, and diarrhea [1, 2]. It is now commonly acknowledged that COVID-19's respiratory

symptoms can range from hardly perceptible to severely hypoxic with ARDS. In the Wuhan study, the interval between the commencement of symptoms and the onset of ARDS was as little as nine days, indicating that the respiratory symptoms can advance quickly. This condition may also be lethal [2, 3]. Patients with severe illnesses have been dying more often across the world. According to epidemiological studies, mortality rates are greater among the elderly population and significantly lower among children [5, 6]. There is currently no effective targeted therapy, and medical management is primarily supportive. Clinical trials have been conducted on several medications, including lopinavir-ritonavir, remdesivir, hydroxychloroquine, and azithromycin, but none of these have yet been conclusively shown to be a treatment for HIV. Clinical trials are being used to test more treatments[7]. Lockdowns and social exclusion have been enacted in many nations to stop the virus from spreading further. Here, we will review what we know about COVID-19, and how it has impacted the kidney and thyroid gland during and after the post-acute phase of the infection.

## 2.2 COVID-19 Global Epidemiological Data

Although other organ systems are also affected, the respiratory system is where SARS-CoV-2 virus primarily manifests itself. The original case series from Wuhan, China, revealed symptoms associated with lower respiratory tract infections, such as fever, dry cough, and dyspnea [1, 2]. In addition, many reported experiencing headaches, vertigo, widespread weakness, vomiting, and diarrhoea [1]. It is already commonly acknowledged that COVID-19's respiratory symptoms are exceedingly high, and up to now several studies have been based on reports of events in China[3]. When the outbreak first started, instances of COVID-19 were primarily found in the elderly. As the outbreak persisted, cases among those 65 and older climbed further, but there was also some evidence of a rise in infections among young children (under 18 years old). Although there were

initially more male patients, there was no discernible gender difference as the number of cases rose[5]. The average time of incubation was 5.2 days. The overall fatality rate per case was 4.9%[4]. Using information from two hospitals in Wuhan, the risk factors of in-hospital death were investigated. The multi-variable analysis revealed that older age, a higher SOFA score (sequential organ failure assessment) score, and d-dimer > 1 g/mL on admission were risk factors. The existence of coronary artery disease, diabetes, and hypertension was also regarded as a risk factor in the univariable analysis. In Wuhan, a study of 85 fatal COVID-19 patients with a median age of 65 years revealed that multi-organ failure was the leading cause of death, accounting for 94%, 81%, and 74% of instances of respiratory failure, shock, and ARDS, respectively. High d-dimer levels, fibrinogen, and protracted thrombin times were observed in severe illnesses, which is consistent with the high prevalence of multiorgan failure[8].

The SARS-CoV-2 outbreak in China has spread worldwide. The United States has the most reported COVID-19 patients as of early April 2020, followed by Spain, Italy, Germany, France, and China. Following the China pandemic, Italy was severely impacted. As in Chinese series, the mortality rate was also greater in the elderly population [9]. The case-fatality rate in the Italian report was 7.2%, which was three times higher than the rate in China. Although Italy had a higher case fatality rate for patients 70 years of age or older, the rates between 0 and 69 years old were very similar in both nations. The high case-fatality in Italy was partially explained by the demographics, since 23% of Italians were 65 years of age or older. There are numerous resources that have data from the US and other nations. Soon, we hope to get more knowledge from various nations[9].

Children made up a relatively modest portion of the COVID-19 patients overall from the beginning of this outbreak. Children under the age of 10 and those between the ages of 11 and 19

made up 1% of all cases, according to statistics from February 2020 provided by the Chinese Agency for Disease Control and Prevention (China CDC) [10] . This may indicate a lower prevalence of COVID-19 in the pediatric population, given that this age group makes up 20% of the entire population. If fewer tests were performed on kids because they had fewer symptoms, this prevalence in the paediatric population might be underestimated. Due to the Chinese New Year holidays, schools in China were closed for most of the pandemic, which may have led to less exposure among youngsters. Asymptomatic, mild, moderate, and severe diagnoses were given to 4.4%, 50.9%, 38.8%, and 5.9% of the 2134 paediatric COVID-19 patients in the China CDC report, respectively [1] . A summary of the terms asymptomatic, mild, moderate, severe, and critical is given. In comparison, adults made up 18.5% of the patient population. The proportion of severe and critical cases was 10.6%, 7.3%, 4.2%, 4.1%, and 3.0% for the age groups of 1, 1-5, 6-10, 11-15, and 16 years, respectively [1] . Babies were most susceptible to severe types of infection. Each of the age groups (0–9) and (10–19) had a zero case-fatality rate. Just 1.2% of COVID-19 patients in Italy were between the ages of 8 and 18. Age groups 0 to 9 and 10 to 19 had case fatality rates of 0% and 0.2%, respectively, which was consistent with Chinese experience [1] . 6.3% of all cases that tested positive for COVID-19 in late March, according to statistics from the Korean CDC, were in youngsters under the age of 19 [11] . The US CDC published research on 2572 COVID-19 cases among children under the age of 18 on April 6, 2020 [12] . Despite making up 22% of the US population, this age group had only 1.7% of all recorded cases in the country. Overall, the findings revealed that, contrary to Chinese stories, youngsters exhibited fewer symptoms than adults. Just 73% of the kids for whom complete data were available experienced fever, cough, or shortness of breath. In contrast, 93% of people between the ages of 18 and 64 reported doing so over the same period. The maximum predicted hospitalization rate for kids between the ages of 1 and 17 was 14%[13]. In contrast, infants made up

the highest proportion of hospital admissions (15-62%), which was consistent with Chinese CDC statistics once more[12]. Despite the pediatric population's overall good fortune, a number of deaths have been reported in the Nigeria and other nations, and more data must be gathered.

There is considerable interest in the correlation between gender and illness severity about COVID-19. Even though there were an equal number of male and female cases in the Chinese series, the data suggested that more men than women died from severe illness[14]. The statistics from other nations showed comparable outcomes. Comorbidities, including hypertension, cardiovascular disease, and lung illness, were linked to negative COVID-19 results. These illnesses are more common in men and are connected to smoking and alcohol consumption[15]. Another hypothesis suggested was sex-based immunological variations. Additionally, the study that looked at factors influencing the adoption of protective behaviors, specifically in the context of pandemics, discovered that women were about 50% more likely than men to practice non-pharmaceutical behaviors, such as hand washing, using a face mask, and avoiding crowds, which may be partially to blame[16].

### 2.2.1 Epidemiology of COVID-19 in Nigeria

Throughout the time of the study, 2,058 deaths were reported in Nigeria overall[17]. This value ranked Nigeria as the 79th most affected country globally, accounting for 0.07% of COVID-19-related deaths, and the 7th most affected African country in terms of COVID-19 related deaths, just behind South Africa (52,648), Egypt (11,845), Tunisia (8,705), Algeria (3,077), Ethiopia (2,784), and Kenya (2,104)[18]. The United States (543,003), Brazil (307,112), Mexico (300,862), and India (161,552), which is at the top of the mortality ranking, all achieved levels that are significantly below those found in the Americas and Asia[17, 19].

The cumulative death rate in Nigeria is one per 100,000 people after population adjustment. As compared to other African nations like South Africa (88.8), Tunisia (73.7), Eswatini (57.4), Cape Verde (29.7), and Botswana, this rating is extremely low (21.5). Nigeria now ranks 153rd globally in terms of the total number of deaths per 100,000 people. The United Kingdom (186.4), Mexico (155.8), Brazil (144.5), France (143.8), and India all recorded higher numbers (11.7)[20].

Throughout the study period, Nigeria had a cumulative case fatality rate of 1.30%. This figure is less than the 2.2% (2,769,473/129,359,540) global case fatality rate as of April 6. Yemen (21.0%), Mexico (9.5%), Syria (6.7%), Sudan (6.5%), Egypt (5.7%), Ecuador (5.2%), China (4.7%), Bolivia (4.5%), Somalia (4.5%), Afghanistan (4.3%), Zimbabwe (4.1%), Liberia (4.1%), Tanzania (4.1%), and Bosnia and Herzegovina (3.8%) have recorded higher levels (18, 20). In general, sub-Saharan Africa has a lower-case fatality rate for COVID-19 than the Americas, Asia, Europe, and North Africa (apart from a few rare occurrences)[18].

Many of the confirmed cases were younger, between the ages of 25 and 39 [15, 16]. The fact that youth make up more than 60% of Nigeria's population may help to explain this [18]. Furthermore, of the COVID-19 confirmed cases in Nigeria, children under the age of 5 and those between the ages of 5 and 9 accounted for 1.26% and 1.65%, respectively. Although there isn't a clear explanation for why COVID-19 is more common in children, some writers have proposed that the immune systems of children may work differently[19].

In Nigeria, the COVID-19 infection pattern showed a male preponderance, according to gender stratification. This finding is consistent with a prior report from the African Region of the World Health Organization and research from China and Italy [16]. This preference for men has been attributed to genetic and physiological causes, including the fact that men have a greater distribution of the SARS-CoV-2 cellular receptor and angiotensin-converting enzyme 2 (ACE-2)

than do women[21, 22]. From another angle, males in Nigeria's highly patriarchal society are more likely to put up with socioeconomic activities outside of the home, increasing their risk of exposure to COVID-19.

Lagos State and the Federal Capital Territory were far and away the top of the table, accounting for over half (47.48%) of the total COVID-19 pandemic in Nigeria [20]. There was substantial heterogeneity in the incidence of COVID-19 among the other states in Nigeria and the Federal Capital Territory. This is hardly shocking considering that the two busiest airports in the nation serve the most Nigerian destinations in both states [23]. The volume of international travel in the states, the variety in population in each state, the difference in testing capacities of each state, and primarily the heterogeneous makeup of the Nigerian state can all be used as causes for these discrepancies[18, 23].

In comparison to the Americas, Asia, Europe, and North Africa, Sub-Saharan Africa has a relatively low incidence of COVID-19 (except from a few individuals) [16, 17]. Africa had already been identified as the continent that is most susceptible to COVID-19 infection and mortality, as well as the area where the virus will have the most impact. The continent's poor healthcare infrastructure and sizable population of immunocompromised people served as the foundation for the projection[24, 25]. The current situation contradicted the prognosis, though. Some researchers have explained the minimal air traffic, the huge number of young people living there, the good environment, their immunity from earlier vaccines, and the poor reporting of incidents as the reasons for the limited impact of COVID-19 in the area[23].

The COVID-19 trend in Nigeria revealed a bimodal tendency. The second surge, which represents the second wave of COVID-19, demonstrates a pandemic that restarted after flattening.

### 2.2.2 Epidemiology of COVID-19 in Ibadan

On March 17, 2020, Oyo State noted her first COVID-19 case as a returnee from the United Kingdom. The Oyo State Ministry of Health responded rapidly to manage the outbreak with the aid of technical and development partners [25] . There were 143 fatalities out of a total of 8,990 confirmed cases (CFR: 1.6%). There were 4,512 men overall, or 50.2%. With a range of 0 to 108 years, the mean age was 39.0 17.3 years. Those under 70 years old had the greatest age-specific CFR (ASCFR) (ASCFR: 9.6%). All 33 LGAs were impacted, with Ibadan-North having the highest incidence (1,995 cases, or 22.3%), and attack rate (795.2 per 100,000 population). In the first wave, the CFR climbed to 1.6%; in the second wave, it increased to 2.4%; and in the third wave, it dramatically decreased to 0.8%. The second wave saw an increase in COVID-19 cases among females, those under the age of 20, and urban dwellers. Only 545 people (7.2%) had time to testing of less than a day. For the period, Oyo State had a COVID-19 prevalence of 0.098%[25, 26].

When compared to outbreaks occurring simultaneously in Lagos, the Federal Capital Territory, and Kano States in Nigeria, it may be claimed that the outbreak in Oyo State is minor. Nonetheless, instances were found in one significant urban LGA (Local Government Authority) in the center of Ibadan, the capital of Oyo State, in terms of dissemination[26, 27]. The majority of COVID-19 cases in the current outbreak, which has been documented in Lagos and Kano States and other nations, were in major cities; however, there were also cases in rural regions. The epidemic curve initially displays a conventional pattern of propagation, followed by an unusual point source [26, 27] . This goes hand in hand with the epidemic curve that was outlined in the outbreak in China that followed a typical point source pattern. The median incubation period we

found is in line with how long COVID-19 has been known to incubate. The two cases in the current outbreak contributed to the initial wave of illness[26, 27].

### 2.3 Mechanism of Action of COVID-19

The structural proteins nucleocapsid (N), membrane (M), envelope (E), and spike (S) make up the coronavirus virion. The S glycoprotein mediates the viral particles' entrance processes, which include fusion and adhesion to the host cell membrane[28]. The virion's membrane is filled with numerous copies of the S protein, which is assembled as a homotrimer and gives it a crown-like look. Several viruses, including the HIV-1, Ebola, and avian influenza viruses, break their entry glycoproteins into two subunits: extracellular and transmembrane (that is, the cleavage occurs before release of the virus from the cell that produces it)[28, 29, 30]. Similar to this, while the S protein of other coronaviruses is only cleaved when it reaches the next target cell, the S protein of other coronaviruses is split into S1 and S2 subunits during their manufacture in the infected cells[28, 30]. The S protein of SARS-CoV-2 and MERS-CoV is cleaved by proprotein convertases like furin in the virus-producing cells, placing them in the first category. Consequently, the S protein on the mature virion consists of two non-covalently linked subunits: the S1 subunit binds ACE2 while the S2 subunit fixes the S protein to the membrane. A fusion peptide and other components required to promote membrane fusion during infection of a new cell are also included in the S2 subunit[28, 29].

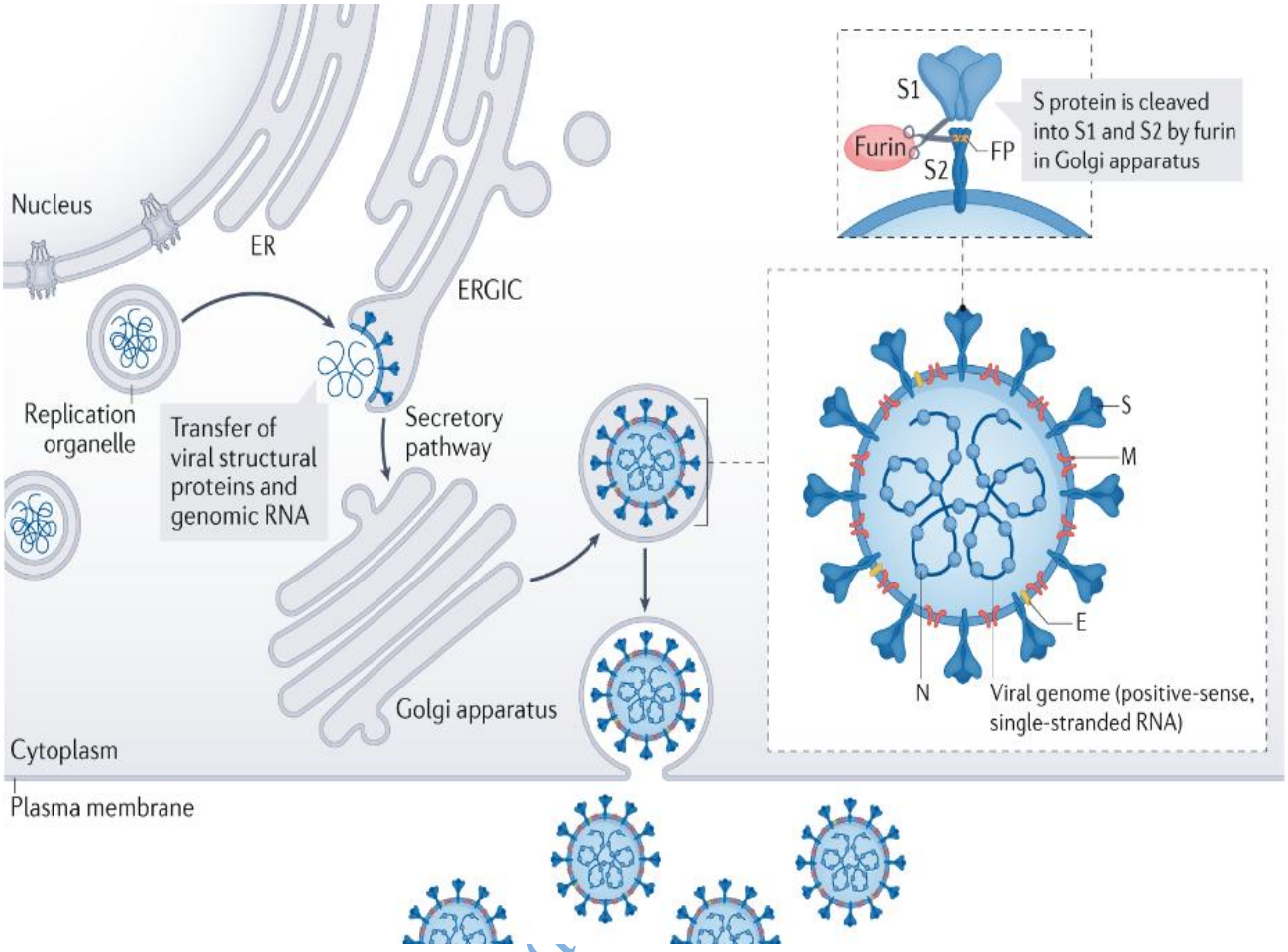


**Fig. 2.1: Coronavirus Structure and Maturation[28].**

Source: Free PMC Article, 2020.

When receptors are activated by viral entry glycoproteins—typically in conjunction with other triggers—dramatic conformational changes are induced in both subunits, fusing the viral and cellular membranes, and resulting in the creation of a fusion pore that permits the viral genome to enter the cell cytoplasm[30]. The trigger for SARS-CoV-2 is the cleavage of an extra internal site known as the "S2′ site" within the S2 subunit. The virus exposes the S2′ location by engaging ACE2. By releasing the fusion peptide following ACE2-mediated endocytosis, S2′ site cleavage by transmembrane protease, serine 2 (TMPRSS2)12, 13, 14 at the cell surface or by cathepsin L15, 16 in the endosomal compartment causes fusion pore formation[29]. Every step of this process is crucial because the viral genome needs access to the cytoplasm and can only do so as this pore widens and the viral and cell membranes meld together[29, 30].

The spike protein is cleaved by a protease after SARS-CoV2 binds to the host protein. SARSCoV and MERS-CoV spike protein activation was described as a two-step sequential protease cleavage, with priming at the S1/S2 cleavage site and activation at the S′2 site[30]. At the S1/S2 cleavage site, the S1 and S2 subunits are still non-covalently bound, and the distal S1 subunit helps to stabilize the membrane-anchored S2 subunit at the prefusion state. The spike is apparently activated for membrane fusion by further cleavage at the S′2 location via irreversible conformational changes[29]. The coronavirus spike is distinct from other viruses in that it can be cleaved and activated by a variety of proteases. The presence of a furin cleavage site ("RPPA" sequence) at the S1/S2 site is one of the traits that set SARS-CoV-2 apart from other coronaviruses. In stark contrast to the SARS-CoV spike, which was integrated into assembly without cleavage, the S1/S2 site of SARS-CoV-2 was completely susceptible to cleavage during biosynthesis. Although other proteases, such as transmembrane protease serine 2 (TMPRSS2) and cathepsin L, also cleaved the S1/S2 site, the widespread expression of furin likely contributes to the virus's high pathogenicity[28, 30].

## 2.4 SARS-CoV-2-Associated Immunopathogenesis

Immune responses brought on by SARS-CoV-2 infection include innate immune sensing, innate immune responses, and adaptive immunity. Presently, research on humans and prior knowledge of other coronaviruses, such as SARS-CoV and MERS, are substantially incorporated into our understanding of SARS-CoV-2 immunopathogenesis[31, 32]. Pattern recognition receptors (PRRs) recognize the viral RNA and cause the production of cytokines and chemokines, which is how the innate immune system detects SARS-CoV-2, interferon (IFN), among other cytokines, must be released early and in sufficient quantities to effectively limit viral replication and maintain host life[31]. Many coronaviruses devise methods to evade PRR activation and thwart subsequent IFN responses in order to circumvent innate immune detection. According to a recent study, the SARS-CoV-2 Alpha variation inhibits innate immune responses more effectively than earlier lineages[31, 32]. Through decreasing RNA sensing in airway epithelial cells, higher protein levels of Orf9b from the alpha variant interact with TOM70 and reduce innate immune responses[33].

The immune pathogenesis of SARS-CoV-2 is driven by the infected epithelial cells, which launch a potent type-I and III IFN (IFN binds to IFNLR) response and release inflammatory cytokines including IL-6 and IL-1 to attract and activate granulocytes, DCs, and macrophages to the lung [33]. Additionally, patients with COVID-19 ARDS have been found to have elevated amounts of hyaluronan, which can be induced by TNF- and IL6. Several recent studies suggested that SARS-CoV-2 stimulates peripheral blood monocytes to elicit inflammatory responses by the release of TNF-, IL-1, and IL-6 despite the absence of productive viral replication in these cells[31, 33]. This is in addition to the direct stimulation of myeloid cells by infected alveolar epithelial cells. Bronchoalveolar lavage fluid from individuals with severe COVID-19 underwent single cell RNA sequencing analysis, which revealed a significant number of proinflammatory

macrophages originating from monocytes[32]. A recent single cell RNA sequencing examination of the bronchial alveolar lavage fluid from ferrets infected with SARS-CoV-2 also discovered several subpopulations of macrophages at 2 days after infection [34] . It is imperative to conduct more research to show how monocytes function in viral eradication and late-stage hyperinflammation. Indicating the complicated nature of the macrophage responses, RNA velocity analysis revealed complex kinetics in both M1 and M2 macrophages that were formed from monocyte-derived macrophages[34].

Natural killer (NK) cells in the lungs, which are innate lymphoid cells that produce type-I IFN (IFN/IFN), as well as IL-12 and IL-18 to support helper T cell responses, play significant roles in limiting viral infection. In the peripheral blood of COVID-19 patients, NK cell numbers have been found to be lower in several investigations, although it is yet unknown if this is due to NK cell recruitment to the pulmonary milieu [35, 36] . Functionally, COVID-19-infected individuals' peripheral blood NK cells displayed a less activated status with possible reduction in cytotoxicity and chemokine/cytokine production[37, 38, 39]. There is currently no proof that SARS-CoV-2 infects NK cells directly[40, 41]. Hence, the elevated expression of inhibitory or immunological checkpoint molecules including LAG3, TIM3, and NKG2A in NK cells from COVID-19 patients may help to partially explain the abnormal activation status. Little research has been done on other innate lymphoid cell populations, namely ILC1/2/3, in SARS-CoV-2 infection [42, 43] . Therefore, more focus should be placed on these cells in the immunopathogenesis of SARS-CoV-2 infection because of their significant contribution to the quick innate immune response to infections[39, 42, 43].

SARS-CoV-2 immunopathogenesis and control are greatly aided by adaptive immunity. Blood from COVID-19 patients frequently shows lymphopenia, and the degree of lymphopenia relates to the severity of the illness [44, 45] . Although the exact cause of COVID-19 lymphopenia is

currently unknown, it has been proposed that lymphocyte recruitment to the infected lung may play a role[44, 45, 46]. Patients with COVID-19 had peripheral blood and bronchial alveolar lavage fluid with SARS-CoV-2-reactive CD4 and CD8 T cells. The population of regulatory T cells and T cells is diminished in individuals with severe COVID-19, pointing to insufficient immunological control and viral defence[43, 44, 46, 47]. Similar to this, peripheral CD8 T cells from individuals with severe COVID-19 have decreased cytotoxicity as seen by decreased CD107a and Granzyme B expression. It should be noted that the phenotype and activity of CD8 T cells in infected lungs differ from those seen in peripheral blood because they express more cytotoxic genes in bronchial alveolar lavage (BAL) CD8 T cells[42, 43]. To address the functional importance and mechanism of the disparity, further work will be required. In addition to T cells, B cells play a crucial role in the creation of antibodies that neutralize viral infections. Most COVID-19 patients have been shown to have SARS-CoV-2-specific antibodies, plasma cells, and memory B cells, despite the fact that there is no compelling evidence linking antibody titers to illness severity [43, 45, 47] . It is fundamentally unknown how long-lasting the B cell immunity against SARS-CoV-2 is in preventing viral reinfection because of its recent development. However, information from the SARS-CoV-1 and MER-CoV revealed that the typical duration of protection is at least 2 to 3 years. However, it is unlikely that the neutralizing antibodies will prevent reinfection as efficiently as they did the previous time due to the introduction of several SARS-CoV-2 virus types[48, 49].

**Table 2.1: Clinical Features of COVID-19[3].**

| | |
|---|---|
| Asymptomatic | COVID nucleic acid test positive. Without any clinical symptoms or signs and the chest imaging is normal |
| Mild | Symptoms of acute upper respiratory tract infection (fever, fatigue, myalgia, cough, sore throat, runny nose, sneezing) or digestive symptoms (nausea, vomiting, abdominal pain, diarrhea) |
| Moderate | Pneumonia (frequent fever, cough) with no obvious hypoxemia, chest CT with lesions. |
| Severe | Pneumonia with hypoxemia (SpO2 < 92%) |
| Critical | Acute respiratory distress syndrome (ARDS), may have shock, encephalopathy, myocardial injury, heart failure, coagulation dysfunction and acute kidney injury. |

Source: Journal of Advanced Research, 2020[3]

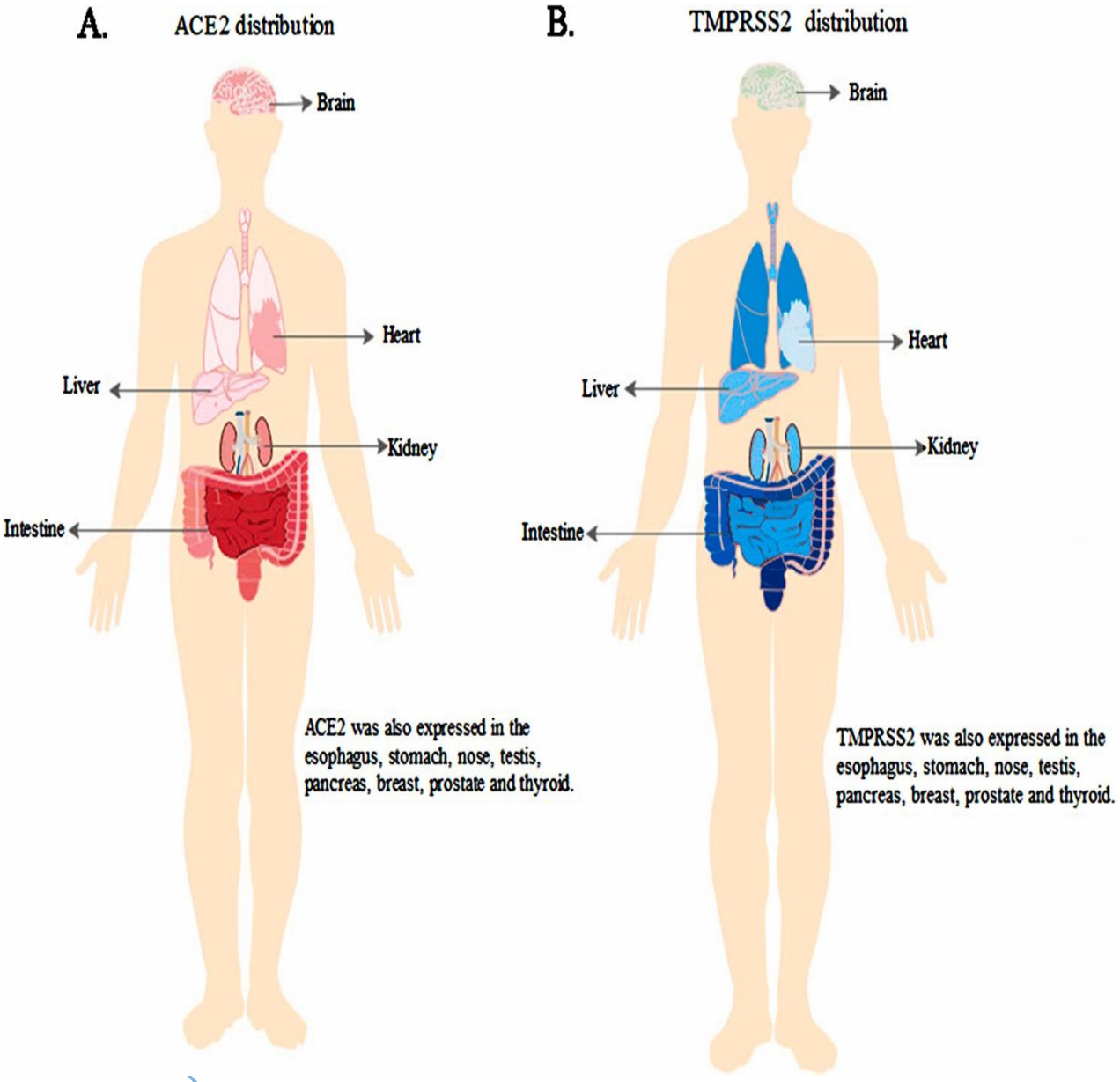


**Figure 2.2. ACE2 and TMPRSS2 mRNA Expression in Extrapulmonary Organs.**

Source: Cell Transplantation, 2020[50].

## 2. 5 ACE2 and TMPRSS2 mRNA Expression in Extrapulmonary Organs

It's crucial to research the extrapulmonary organs' viral vulnerability in order to comprehend the pathogenesis of SARS-CoV2 infection. Research has demonstrated that ACE2 and TMPRSS2 were expressed in extrapulmonary organs in addition to lung cells and tissues[50, 51]. The levels of ACE2 and TMPRSS2 expression in extrapulmonary organs, such as the heart, kidney, liver, digestive tract, brain, and thyroid gland, were reviewed in this section.

### 2. 5.1 Kidney

The epithelium of the kidney shows an elevated level of ACE2 expression[50, 51]. An increase in salt reabsorption, an increase in blood volume, an increase in blood pressure, and kidney injury can all result from the loss of ACE2 or internalization of ACE2 in the kidney[50]. Patients who are admitted to the hospital for COVID-19 have an increase in protein in the urine (proteinuria), and there is more blood in the urine, according to preliminary data on kidney function (hematuria)[52]. People who have a severe COVID-19 clinical course had higher levels of circulating renin, ANG II, and aldosterone than those who experience a mild COVID-19 clinical course[50, 53]. Moreover, acute kidney damage (AKI) affects roughly 36.6% of individuals with SARS-CoV-2 infection[54]. AKI is more common, especially in ventilated patients. SARS-CoV-2 viral load testing on autopsied COVID-19 patients revealed the viral genome was present in the kidneys, specifically in the renal tubule cells and glomeruli cells. By controlling the kidneys' filtration process, the glomeruli, and tubular cells work together to maintain homeostasis. Moreover, COVID-19 patients' urine samples have also contained SARS-CoV-2 virus particles[1, 55].

The Genotype-Tissue Expression GTEx database's expression study revealed that kidney expressed ACE2 at the sixth highest level[56, 57]. The public single-cell transcriptome dataset of healthy donors' normal kidneys was used to study the expression of ACE2 in the kidney. The

findings revealed that angiotensin converting enzyme-2 (ACE2) was distributed throughout a variety of cell types but was primarily enriched in proximal tubule cells [58]. The findings were verified using Gene Expression Omnibus (GEO) dataset's that tubular cells express angiotensin converting enzyme-2 (ACE2) specifically, but immune cells and glomerular parietal epithelial cells do not. The Cancer Cell Line Encyclopedia (CCLE), GTEx database, and Human Protein Atlas dataset were three online databases from which RNA and protein expression data of angiotensin converting enzyme-2 (ACE2) in various human tissues and cancer cell lines were obtained. The results showed that both mRNA and protein expression levels of angiotensin converting enzyme-2 (ACE2) were relatively high in kidney cells; especially in renal tubular cells[59]. Meanwhile, it was also discovered that either proximal tubular cells or tubular progenitor cells in the kidney co-expressed angiotensin converting enzyme-2 (ACE2) and Transmembrane serine protease 2 (TMPRSS2) in scRNA-Seq datasets of kidney tissues. The scRNA-seq data from the GEO dataset (GSE134355) revealed that the expression levels of ACE2 and TMPRSS2 were high in the kidney's nephron epithelial cells, epithelial cells, endothelial cells, and mesangial cells[60]. Recently, it was discovered that kidney podocytes co-expressed the TMPRSS2 and ACE2 genes. Hence, we can deduce from our review that using the stated findings that it is confirmed that renal tissues and cells both produced significant levels of ACE2 and TMPRSS2[61].

### 2.5.2 Thyroid Glands

In two primary thyroid cell cultures and 15 distinct thyroid tissue specimens, the expression levels of ACE-2 mRNA were assessed [62]. All thyroid tissue samples contained ACE-2 mRNA. The average transcript expression levels for GAPDH and -actin were compared to those for ACE-2 mRNA (two reporter genes ubiquitously expressed by cells) Large levels of ACE-2

mRNA were found, as indicated in Fig. 2.3 (GAPDH: 0.052 0.0026 Cycles1; -actin: 0.044 0.0025 Cycles1; ACE-2: 0.035 0.0024 Cycles1)[62]

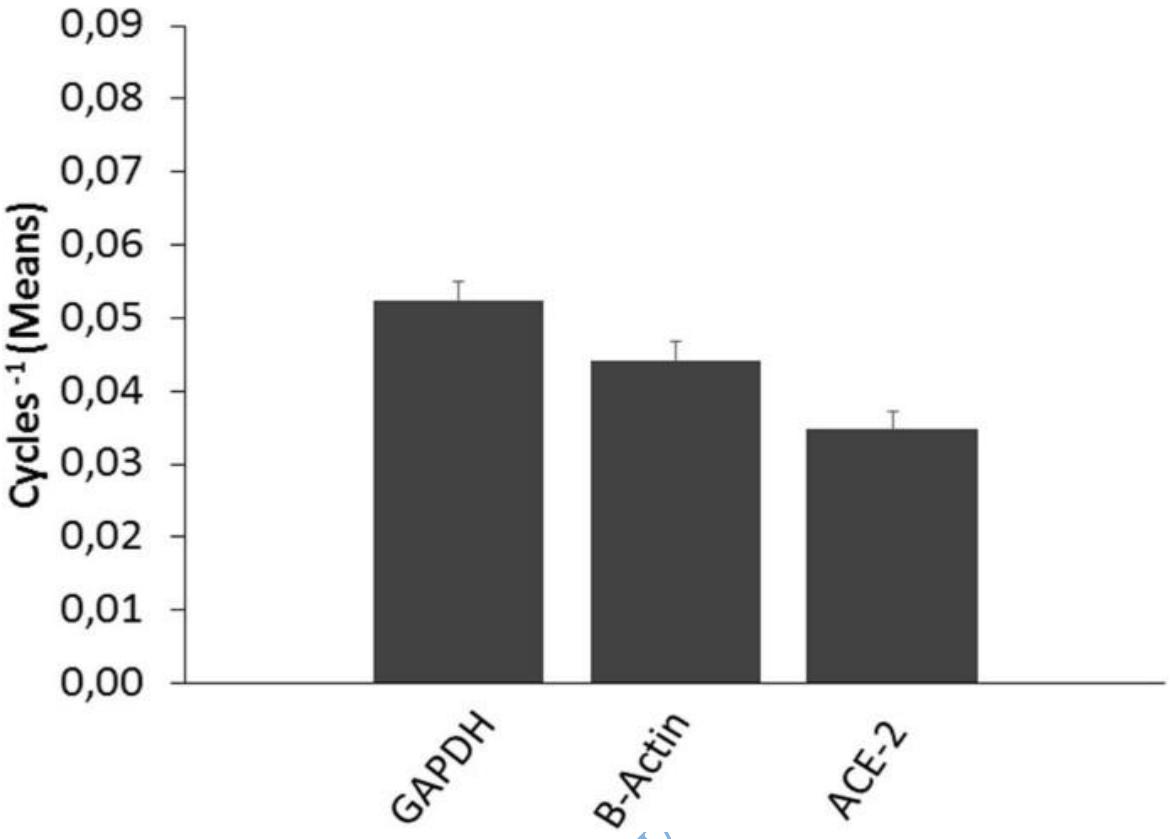


**Fig. 2.3: Mean Expression of ACE-2 in Thyroid Tissue Specimens**.

Source: Journal of Endocrinological Investigation, 2021.

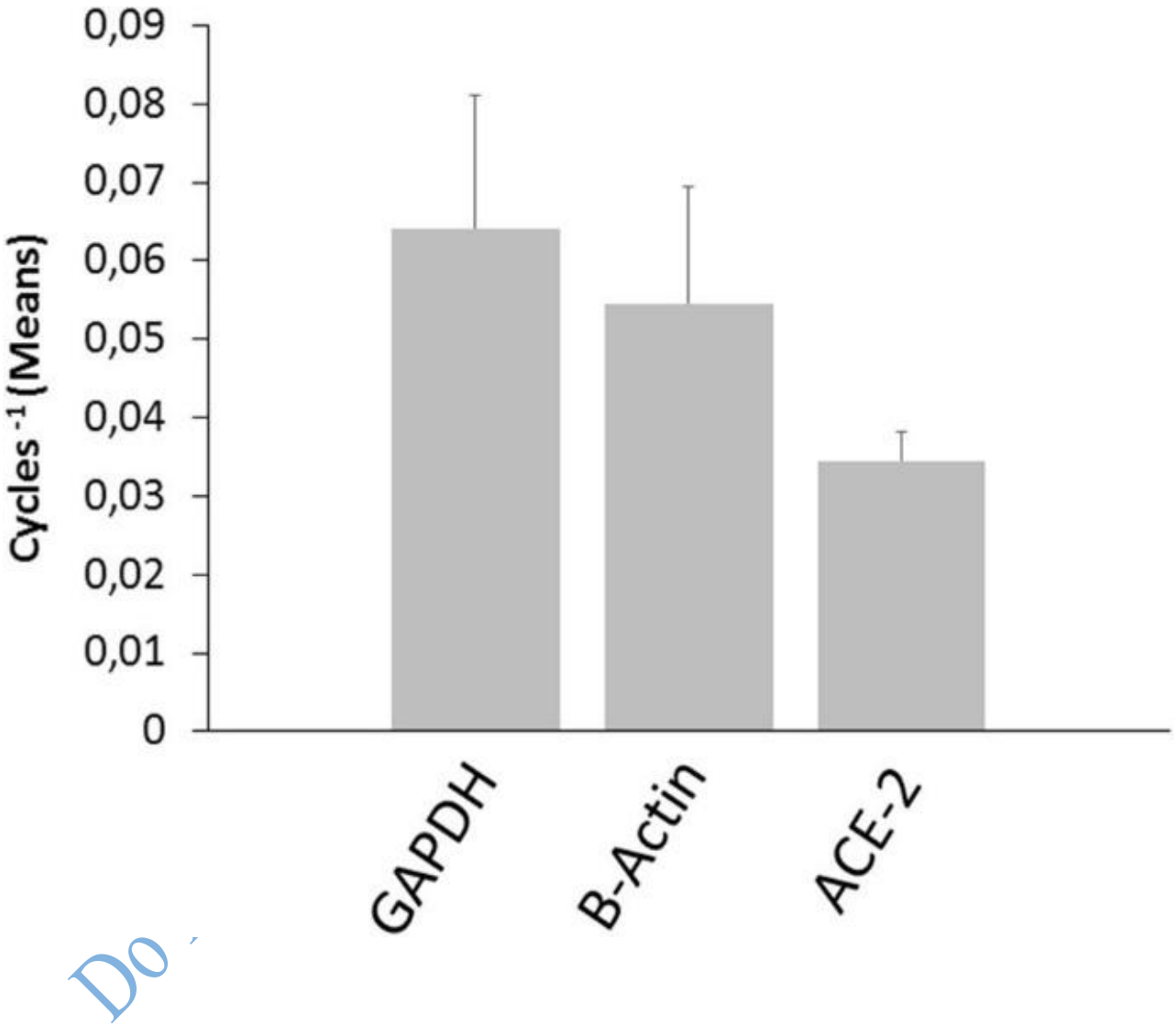


**Fig. 2.4: Mean Expression of ACE-2 in Primary Cultures of Thyroid Cells.**

Source: Journal of Endocrinological Investigation, 2021.

Primary cultures of thyroid cells were also examined to confirm the expression of ACE-2 mRNA by follicular cells (Fig. 2.4). It's interesting to note that in primary culture, follicular thyroid cells and thyroid tissue specimens had superimposable ACE-2 mRNA expression levels. These results suggest that the total RNA isolated from tissues and reverse transcribed into cDNA came primarily from follicular thyroid cells. Furthermore, the 15 thyroid tissue samples showed no discernible differences in the ratio of the ACE-2/GAPDH mRNAs, which is related to -actin. When the ACE-2/-actin ratio was measured as a percentage of GAPDH, the same outcome was seen. When combined, the results above blatantly demonstrate a general between-patient homogeneity for the levels of mRNA encoding the ACE-2 gene expression.

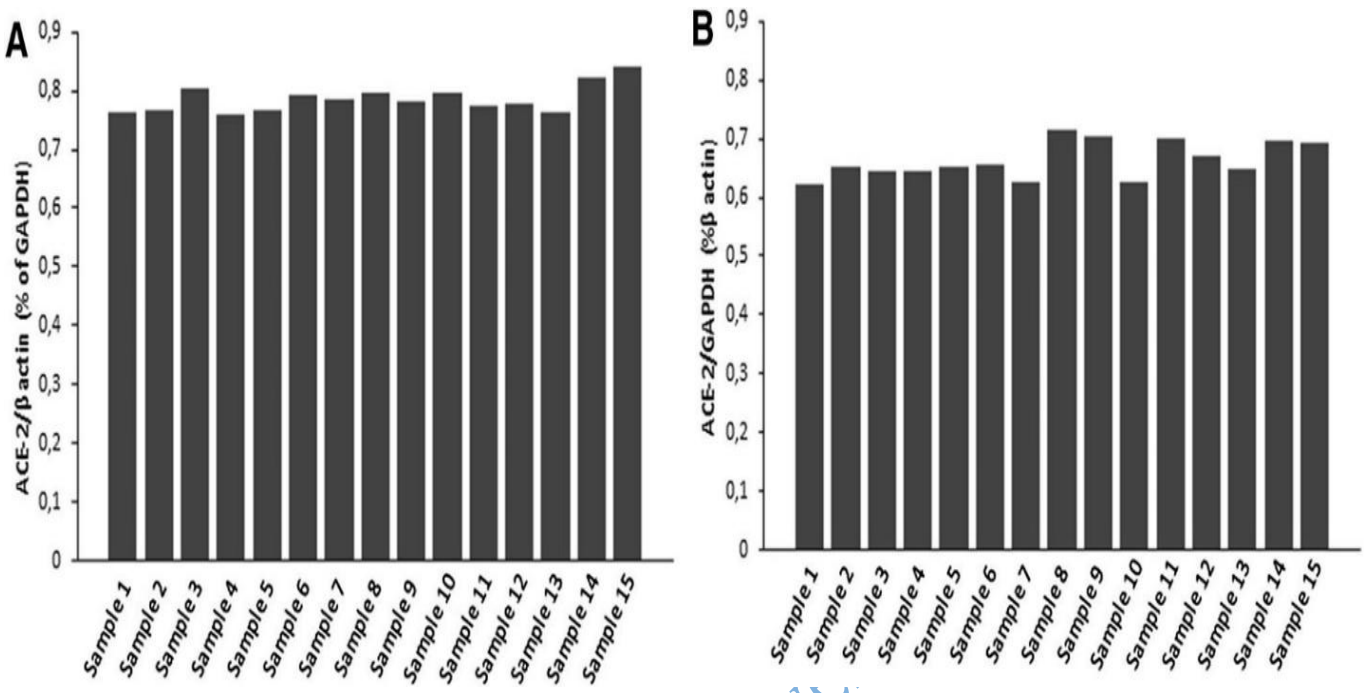


**Fig. 2.5** Panel (**A):** ACE-2/β-actin ratio calculated as percentage of GAPDH. Bars are representative of distinct thyroid tissue specimens.

Panel **(B)**: ACE-2/ GAPDH ratio calculated as percentage of β-actin[63].

Source: Pathogens (Basel, Switzerland), 2019**.**

The ACE-2 mRNA is consistently expressed in thyroid tissue specimens and cells, according to RT-PCR results. The expression of ACE-2 mRNA in thyroid cells was discovered to be plentiful and, more critically, homogenously expressed when compared to the expression of two distinct transcripts, such as GAPDH and -actin. It is significant to note that, as was just shown, SARS-CoV-2 infection necessitates the coexistence of type II serine protease trans-membranes and the ACE-2 receptor (TMPRSS2). In silico studies suggest that thyroid tissues, without gender differences, demonstrate a high expression of the TMPRSS2 mRNA. All this indicate that the mRNA encoding for the ACE-2 receptor is expressed in follicular thyroid cells, making them a potential target for SARS-COV-2 entry[63].

### 2. 5.3 Heart

The heart was found to express ACE2 when the mRNA expressions of ACE2 in several human organs were examined. Moreover, it has been investigated how ACE2 was expressed in several cardiac cell types and discovered that pericytes were the only cells that express ACE2 [57] . Additionally, myocardial ACE2 expression was found to be significantly higher in patients with heart failure when RNA sequencing was performed on 40 patients with failing hearts and 15 normal donors. This finding was confirmed at the protein level by proteomics profiling of 8 patients with failing hearts and eight healthy donors [57] . Another study found that patients with underlying heart disease had higher levels of ACE2 expression in their heart tissues compared to healthy heart tissues. According to these two studies, the expression of ACE2 was higher in heart tissue from patients who had underlying cardiac disease than it was in heart tissue from healthy individuals [64] . The (GTEx) database was used to examine the mRNA expression of TMPRSS2, and the results revealed that TMPRSS2 is also expressed in the heart [65] . Single-cell RNA sequencing (scRNA-Seq) was used to assess the gene expression landscapes of 4000 cardiac

cells from human embryos. Likewise, it was revealed that the cardiovascular progenitor cells and cardiomyocytes have correspondingly higher and lower percentages of ACE2- and TMPRSS2-expressing cells [64, 66, 67]. These findings demonstrated that the heart expressed both ACE2 and TMPRSS2.

### 2. 5.4 Digestive Tract

Angiotensin converting enzyme-2 (ACE2) was discovered in the upper esophagus, as well as in the stratified epithelium cells and absorptive enterocytes of the ileum and colon, according to a prior study [66]. Quantitative mRNA expression profiling of ACE2 across 72 human tissues showed that ACE2 was expressed at a high level in gastrointestinal tissues [68.]. Single-cell transcriptome data from the esophagus, gastric ileum, colon, and lung were analyzed; the results revealed that ACE2 was highly expressed not only in the type II alveolar cells (AT2) of the lung but also in stratified epithelial cells, ileum absorptive enterocytes cells, and colon enterocytes [69]. Similar to this, gastrointestinal epithelial cells' cytoplasm was mostly stained for ACE2 by immunofluorescent labeling of the esophagus, stomach, duodenum, and rectum. Additionally, the scRNA-seq data revealed that both the proximal and distal enterocytes had significantly higher levels of ACE2. The colon, stomach, small intestine, and esophagus were among the digestive tract organs with the highest levels of TMPRSS2 expression [65]. Further analysis of seven internal normal colon samples and published scRNA-seq data revealed that the small intestine and colon were the two organs where ACE2 and TMPRSS2 transcripts were most commonly found co-expressed. Among the intestinal cell types, enterocytes had the greatest expressions of TMPRSS2 and ACE2 [70]. These findings demonstrated that the digestive system expresses significant levels of TMPRSS2 and ACE2.

### 2. 5. 5 Pancreases.

It has been established that COVID-19's specific comorbidity of diabetes mellitus (DM) exists[71]. 173 people with severe disease in a study of 1,099 verified COVID-19 patients showed a greater probability of DM than the patients without severe disease [72]. A small study with 39 patients suggested that COVID-19 may enhance the incidence of induced DM. Additionally, a larger study with 72,314 COVID-19 cases revealed a higher mortality rate in DM patients[73].

Patients who had DM and COVID-19 have been associated with the involvement of ACE2 [71]. Until recently, the link between DM and ACE2 has been limited. Yet, because to the availability of substantial datasets condensed from genome-wide association studies (GWAS), scientists can link countless particular genetic variants to certain diseases [74]. Mendelian randomization phenome wide association studies (PheWAS) can effectively screen for potential disease risk factors using the GWAS data. In fact, PheWAS has been used to investigate the conditions and characteristics that are causally related to elevated ACE2 expression in the lungs. By this technique, it is noted that DM is causally associated to increased ACE2 expression [75]. Also, a population-based, prospective epidemiological association study including over 28,000 people found that patients with DM have higher levels of furin, the protease that makes it easier for viruses to enter human cells. As a result, these extensive database-type investigations suggest that individuals with DM may actually be more vulnerable to SARS-CoV-2 infection[77].

In the pancreas, ACE2 is expressed at the site of insulin production. Deficiency of ACE2 in obese mice was observed to reduce b-cell mass and proliferation in tandem with a significantly reduced pancreatic islet area[76, 77, 78]. Loss of ACE2 has been linked to decreased insulin secretion and alterations in glucose tolerance. It was previously demonstrated that immunostaining for

ACE2 was strong in the pancreatic islets and weak in the exocrine cells, suggesting that the SARS coronavirus may enter islet cells using ACE2, and, therefore, may damage islets, which may cause acute insulin-dependent DM [77] . Although further evidence is needed, pancreatic damage may also be present in patients with COVID-19, possibly contributing to worse outcomes of patients with DM [77, 79] . Defining the characteristics and extent of the bidirectional relationship between diabetes and COVID-19 for both those with preexisting diabetes as well as new-onset, COVID-19-related diabetes is the collaborative goal of a Global Registry of COVID-19 related diabetes[80].

### 2. 5. 6 Nervous System

Glial cells, neurons, and spinal fluid are the only parts of the brain where ACE2 is expressed[75, 81]. Brain-derived neurotrophic factor, a potent nerve growth factor required for the proliferation and differentiation of sensory and sympathetic neurons, was found to be lower in mice with ACE2 deletion, which was found to be associated with a decline in cognitive function. This decline was elicited by increased reactive oxygen species generation [75] . Moreover, ACE2 regulates baroreflexes in the brain, and its inhibition or local deletion results in a reduction in baroreflex sensitivity. These results support studies that link neurogenic hypertension—an increase in blood pressure brought on by a dysregulation of neurally mediated sympathetic and endocrine mechanisms—and ACE2 deficiency[75].

Neurons within the brain have been demonstrated to be targeted by SARS-CoV. SARS-CoV infects the brain through the olfactory bulb, which enables the virus to quickly spread throughout the brain, according to in vivo investigations carried out on mice that are transgenic for ACE2. The mice die as a result of the severe neural infection that is brought on by this. Patients infected with SARS-CoV-2 have reported an altered sense of smell, which could be related to the virus

entering through the cribriform plate of the ethoid bone that protects the olfactory bulb, a neural structure responsible for transmitting smells from a person's nose to the brain[82].

SARSCoV-2 has been demonstrated to have a significant impact on brain tissue through examination of infected people. COVID-19 victims who died have partial neuronal degeneration and edematous brain tissue, according to autopsies [82]. According to a study of 214 COVID-19 patients, 36% of them display various neurovascular symptoms that can affect the central nervous system, the peripheral nervous system, or the musculoskeletal system [83]. Patients with COVID-19 in severe condition exhibited more neurological symptoms than those in noncritical condition, according to the American Thoracic Society's recommendations for community-acquired pneumonia[84].

Both TMPRSS2 and ACE2 are expressed at relatively low levels in the cerebral cortex, according to analysis utilizing the GTEx database [51]. Using seven brain transcriptome datasets discovered that ACE2 was relatively highly expressed in some significant brain regions, including the substantia nigra and brain ventricles. High levels of ACE2 expression were found in the piriform cortex of the human brain, and it was also found in many excitatory and inhibitory neurons, as well as some astrocytes and oligodendrocytes, in the middle temporal gyrus and posterior cingulate cortex [57]. ACE2 and TMPRSS2 were both expressed in the oligodendrocyte precursor cells and the astrocytes of the substantia nigra and cortex of the brain, according to the analysis of the scRNA-seq data of the brain's substantia nigra and cortex from the GEO database. There are few reports on ACE2 and TMPRSS2 expression in the peripheral nervous system [85]. Using data from the human scRNA-seq dataset (GSE139522), analyzing the expression of ACE2 and TMPRSS2 in various cell types and discovered that neither olfactory sensory neurons nor olfactory bulb neurons expressed these two genes, whereas ACE2 and

TMPRSS2 were expressed in non-neuronal cells such as sustentacular cells and olfactory bulb pericytes. These findings demonstrated that the nervous system could also co-express ACE2 and TMPRSS2[85].

### 2. 5. 7 Liver

To assess the amount of ACE2 gene expression in the liver, the scRNA-seq data from the GEO database (GSE124395) evaluated. The findings revealed that ACE2 was strongly expressed in cholangiocytes, with a level that was almost 20 times higher than that in hepatocytes. Moreover, the GTEx database revealed that the liver expressed both ACE2 and TMPRSS2 [86] . From the Human Cell Atlas database, it was determined that TMPRSS2 is significantly expressed in hepatocytes[87]. Using scRNA sequencing, it was recently found that TROP2+ hepatic progenitors of human liver tissue selectively co-express ACE2 and TMPRSS2. This suggest that whereas TMPRSS2 is present in hepatocytes, ACE2 expression is expressed at a relatively low level in hepatocytes and is primarily found in cholangiocytes[88].

### 2.5.8 Oral Cavity and Tongue

The SARS-CoV-2 infection symptoms are primarily respiratory in nature; hence COVID-19 is primarily spread through liquid droplets produced in the nose and oral canals [87, 89] . Although no severe symptoms from positive COVID-19 patients involve the oral cavity, researchers are exploring the potential of SARS-CoV-2 infection within the oral cavity [90] . The ACE2 gene is expressed in oral mucosa and is enriched in oral epithelial cells, according to RNA-seq profiles from two public databases, including The Cancer Genome Atlas (TCGA) and Functional Annotation of The Mammalian Genome Cap Analysis of Gene Expression (FANTOM5 CAGE). These profiles were later recognized and verified by single-cell transcriptomics from an independent data source [91] . The tongue epithelium, the fungiform, and the surrounding papillae

were discovered to be the areas with the greatest degree of ACE2 expression out of the 32 distinct oral sites examined. The data show that the oral mucosa may be a possibly high-risk channel for SARS-CoV-2 infection. Angiotensin II can be quickly broken down by the ACE2 enzyme because it is found in oral tissue and taste buds, according to studies in mice. The ACE receptor is also involved in short-term regulation of taste sensitivity through a local RAAS enzyme and plays a functional role in homeostatic pathways both systemically and locally[88, 91].

Two interesting clinical symptoms often associated with milder cases of COVID-19 include ageusia (loss of taste) and anosmia (loss of smell) [92, 93] . To assess olfactory and gustatory disorders induced by SARS-CoV-2, an international multicenter study involving 12 hospitals evaluated 417 patients with confirmed SARS-CoV-2 infection. The study utilized questionnaires on olfactory and gustatory changes, based on the National Health and Nutrition Survey and the short version of the Questionnaire of Negative Declarations of Olfactory Disorders. Briefly, the report revealed that 85.6% and 88.0% of the patients, respectively, reported gustatory and olfactory disorders[94].

More research is necessary to understand why the oral cavity exhibits so few COVID-19 symptoms despite significant ACE2 expression. There are fewer cases of SARS-CoV-2 infection in youngsters than in adults, according to numerous researches [5] . Since the nasal epithelium is one of the first places where SARSCoV-2 infections occur, ACE2 gene expression was assessed in the nasal cavity. When compared to younger children (4-9yr old; n = 45), older children (10-17yr old; n = 185), young adults (18-24yr old; n = 46), and adults (25yr old; n = 29) all showed higher levels of ACE2 in the nasal epithelium. Additionally, there was a notable trend showing that as people aged, their ACE2 expression changed more rapidly. Additionally, it was

discovered that the minor salivary glands expressed ACE2 at a higher level than the lungs, suggesting that saliva samples may be a more accurate diagnostic for SARSCoV-2 infection[95].

### 2.6 Interplay between Thyroid Gland and Renal Organ

Cell growth and protein synthesis are both impacted by thyroid hormones. Research in newborn rats has established the accelerated effect of thyroid hormones on kidney development[96]. The functioning renal mass (calculated as the kidney to body mass ratio) is influenced by thyroid hormone status, with hypothyroidism lowering and hyperthyroidism raising this ratio. Severe hyperthyroidism, however, causes protein degradation and eventually leads to renal atrophy. Congenital renal anomalies are also very common in children with congenital hypothyroidism. The neonatal renal function is also influenced by thyroid hormones[97]. The mitochondrial energy metabolism enzymes in the cells of the proximal convoluted tubules are influenced by the perinatal thyroid hormone status. The Na-P cotransporter (NaPi), Na-H exchanger (NHE), and Na/K ATPase all exhibit increased activity in the PCT. Consequently, thyroid hormones are crucial for renal growth and early renal function[97].

#### 2.6.1 Hyperthyroidism and Renal Function

Hyperthyroidism results in increased renal blood flow (RBF) and glomerular filtration rate (GFR)[98]. The effect of thyroid hormones on RBF and GFR occurs at various levels. Among the pre-renal variables, thyroid hormones boost the cardiac output by positive chronotropic and inotropic effects as well as a reduction in systemic vascular resistance [99]. This indirectly contributes to an increase in RBF. Nitric oxide synthase (NOS) is induced in the renal cortex and medulla, where it is directly influenced by thyroid hormones and indirectly by endothelial shear stress brought on by high arterial pressure. This is accompanied by a reduction in renal vasoconstrictor endothelin. As a result, there is an increase in intrarenal vasodilation and a

decrease in vasoconstriction, which helps to raise RBF overall. Patients with hyperthyroidism experience an 18–25% increase in GFR[100]. This improvement in GFR is not simply attributable to an improved RBF. The increase in GFR is also attributed to the activation of the renin-angiotensin-aldosterone system (RAAS). The RAAS is multifactorially stimulated by thyroid hormones. The density of b-adrenergic receptors in the renal cortex increases along with increasing b-adrenergic activity in hyperthyroidism, which in turn increases RAAS stimulation. Renin gene expression is elevated by 3,3',5-triiodo-L-thyroxine (T3) [101, 102]. Thyroid hormones increase plasma renin, angiotensin II, and serum angiotensin converting enzyme levels. In addition, there is an increase in angiotensinogen synthesis by liver and increased density of angiotensin receptors[103]. As a result, there is a net rise in RAAS activity. As a result, the afferent and efferent arteriolar vasculature dilates and constricts, respectively, increasing the filtration pressure. Beyond what an increase in RBF already contributed, this increases the amount of GFR growth [104] . Hypoperfusion of the proximal convoluted tubule (PCT) and subsequent active sodium and chloride reabsorption in the PCT could be caused by efferent arteriolar vasoconstriction. The apical Na-H exchanger (NHE), the Na-Pi co-transporter, and the basolateral NA/K ATPase all exhibit increased activity. Activation of these transporters increases the proximal sodium reabsorption[105].

With hyperthyroidism, the tubular mass, renal mass, and tubular reabsorption capacity all increase at the same time. The basolateral sodium calcium exchanger is fed by the rise in basolateral sodium content. At the loop of Henle, the avid Cl reabsorption and its transport through the basolateral chloride channel indirectly augment the calcium reabsorption. The distal nephron receives less Cl as a result[102, 106]. The macula densa detects this, which causes the RAAS activity to rise. The macula densa's increased sensitivity in hyperthyroidism leads to further RAAS activity. These effects are undone by treating hyperthyroidism, and the GFR returns to

normal. In addition to an increase in GFR and a decrease in overall muscle mass, hyperthyroid patients' serum creatinine levels, an inverse marker of GFR, are much lower. Cystatin C is a new marker of renal function and a predictor of future cardiovascular risk [103, 104] . It is a cysteine protease inhibitor that is constitutively released by all nucleated cells. Despite an increase in GFR, serum cystatin C levels rise in hyperthyroidism due to increased cell metabolism and cystatin C synthesis. With hyperthyroidism, there is a poor correlation between serum cystatin C levels and GFR. Rebound increases in serum creatinine and drops in serum cystatin C levels occur because of hyperthyroidism treatment[107, 108]. The thyroid status seems to have no effect on urinary neutrophil gelatinase associated lipocalin (NGAL), a promising biomarker of decreased renal function. The glomerular hyperfiltration that reverses with treatment of hyperthyroidism is likely the cause of the 24-hour urine protein rise in hyperthyroidism[107, 108]. Urinary N-acetyl-b-D-glucosaminidase (NAG) is elevated in hyperthyroidism because of tubular damage from hyperfiltration, hypertrophy, and hyperplasia, as well as disruption of the glomerular basement membrane. Instead of vasopressin insensitivity, the decreased ability to concentrate urine is likely caused by increased RBF and osmotic diuresis[101,102]. A reduction in total body water and exchangeable potassium, but not sodium, is linked to hyperthyroidism. The serum sodium and potassium concentrations, on the whole, are normal. Occasionally, genetic mutations in either the potassium inward rectifier or the L-type calcium channel 1-subunit cause hyperthyroidism to be accompanied by hypokalemia (thyrotoxic hypokalemic periodic paralysis of channelopathies)[109, 110].

### 2.6.2 Hypothyroidism and Renal Function

Typically, hypothyroidism has the opposite impact on the kidney as hyperthyroidism does. Reduced cardiac output, increased peripheral vascular resistance, intrarenal vasoconstriction,

decreased renal response to vasodilators, and decreased expression of renal vasodilators like vascular endothelial growth factor (VEGF) and insulin-like growth factor-1 all contribute to the reduction of RBF in hypothyroidism (IGF-1). Reduced RBF may also be caused by pathologic modifications to the glomerular structure in hypothyroidism, such as thickening of the glomerular basement membrane and expansion of the mesangial matrix[96, 97]. More than 55% of individuals with hypothyroidism experience a reversible reduction in glomerular filtration rate GFR (by about 40%) for several different reasons. GFR is lost as a result of decreased sensitivity to -adrenergic stimulation, decreased renin release, decreased angiotensin II, and diminished RAAS action. Due to renal parenchymal development retardation in hypothyroidism, the restricted glomerular surface area for filtration imposes a structural constraint [100, 101]. The proximal tubular absorption of salt, chloride, and water is decreased. Moreover, there is a decrease in the expression of renal basolateral chloride channels. As a result, decreased chloride reabsorption boosts distal chloride supply, resulting in tubuloglomerular feedback that is mediated by the macula densa and lowers RAAS activity[102, 103]. As a result, the GFR decreases. Reduced tubular transport capacity and decreased Na/K ATPase activity first affect the proximal tubules and then practically all nephron segments. In addition, hypothyroidism also results in decreased NHE activity. As a result, there is a net decrease in the reabsorption of sodium and bicarbonate [104]. Urinary acidification is faulty because of increased salt and bicarbonate loss. Reduced tubular reabsorptive capacity also makes it difficult to keep the medullary hypertonicity constant. Urinary concentration is mostly caused by medulla hypertonicity[111]. Lack of medullary hypertonicity in hypothyroidism impairs the kidney's capacity to concentrate urine. Yet, hypothyroidism results in a reversible rise in the collecting ducts' sensitivity to vasopressin (also known as antidiuretic hormone or ADH), which raises the rate of free water absorption[112]. Yet, in hypothyroidism, the increased fluid retention is unable to completely reduce ADH. Pituitary

resistance to the effects of enhanced fluid retention results in sustained ADH activity and more retention of free water. Low cardiac output brought on by hypothyroidism stimulates carotid baroreceptors, which in turn causes an increase in non-osmotic ADH secretion [113, 114] . Some individuals' urine salt levels are not as low as one might anticipate given their decreased cardiac output. It's possible to think of the ADH secretion in these people as being out of place. Hyponatremia in hypothyroidism is caused by lower GFR, decreased sodium reabsorption, substantially elevated ADH output, and renal ADH super sensitivity mediated poor free water clearance [113, 115] . Those with hypothyroidism who have elevated serum creatinine are twice as likely to develop hyponatremia as those who have normal serum creatinine. In hypothyroidism, where the renal mass nearly doubles with treatment, there is a reversible drop in the kidney to body weight ratio. Due to the decrease in GFR, hypothyroidism causes a temporary increase in serum creatinine as well as the potential for myopathy and rhabdomyolysis [116] . Because of decreased production, which leads to decreased cellular metabolism, serum cystatin C levels are reduced in hypothyroidism. With the proper hypothyroidism medication, both alterations are reversible. Increased glomerular capillary permeability to proteins is another effect of hypothyroidism. With hypothyroidism, the resultant proteinuria frequently occurs before the GFR decline[117].

### 2.6.3 Thyroid Dysfunction and Chronic Kidney Disease

Hyperthyroidism can cause or accelerate chronic kidney disease (CKD) in numerous ways. Hyperthyroidism increases intra-glomerular hypertension and hyperfiltration. Secondly, hyperthyroidism causes proteinuria, which damages the kidneys. Lastly, hyperthyroidism-induced mitochondrial energy metabolism and superoxide dismutase downregulation promote free radical production and renal damage [118] . Oxidative stress causes hypertension in

hyperthyroidism, which advances CKD. RAAS activation increases kidney fibrosis. Hyperthyroidism induces anaemia in CKD patients and resistance to recombinant human erythropoietin (EPO). Hypothyroidism only slows CKD progression by lowering GFR. Hypothyroidism treatment improves GFR in CKD patients[112, 118]. CKD patients often have non-autoimmune hypothyroidism. Subclinical hypothyroidism increases with GFR reduction, especially. Low T3 is the first and most prevalent thyroid function anomaly in CKD patients (especially total T3 than free T3). CKD has "low T3 syndrome" for numerous causes. Fasting, metabolic acidosis, and chronic protein deficiency reduce iodothyronine deiodination and T3 protein binding, lowering peripheral thyroxine (T4) to T3 conversion and protein binding[113, 119]. Inflammatory cytokines including TNF-a and IL-1 also inhibit type 1 5′-deiodinase, which converts T4 to T3. Impaired renal iodine processing raises blood iodine levels, prolonging the Wolff – Chaikoff effect. Low T3 syndrome's clinical significance is debatable [119] as different study reported contradicting results. A study that showed most COVID-19 patients had normal thyroid function, with low serum T3 standing out as the most prevalent thyroid abnormality in the acute phase of the disease, seen in 47.3% of patients with severe disease and a significant negative correlation between TSH and the bio-inflammatory marker, C-reactive protein (CRP). CKD patients with low T3 levels (particularly total T3 and not free T3) had higher levels of inflammation markers (high sensitive C reactive protein hsCRP, IL-6, etc.), malnutrition (reduced prealbumin, IGF-1), endothelial dysfunction, poorer cardiac function, poor survival, and higher all-cause and cardiovascular mortality[120]. Several studies were underpowered to find these correlations or did not properly exclude confounders. In some research, low free T3, not total T3, increases mortality. Several investigations have shown that free T3 levels are not always related to long-term mortality in CKD and dialysis patients. CKD patients had decreased T4 levels in subsequent trials. CKD free T4 levels range from low to normal. CKD impairs T4

protein binding. With severe infections, heart failure, cancers, and hospitalized patients without renal disease, the thyroid profile is identical. CKD was considered a "sick euthyroid state," now dubbed "non-thyroidal sickness." CKD does not increase overall (reverse triiodothyronine) rT3, unlike other NTI conditions rT3 redistributes more into extravascular and intracellular areas. Free rT3 may be somewhat higher in patients with poor renal clearance [120, 121] . Thyroid stimulating hormone (TSH) levels are higher in CKD than other NTIs. CKD patients release TSH in reaction to Thyrotropin releasing hormone (TRH), indicating pituitary abnormalities in uremia. CKD alters TSH's circadian rhythm and glycosylation, reducing its activity [(121)] . Consequently, CKD patients have low T3 and T4, raised TSH, and increased thyroid gland volume. These pathways may indicate CKD's physiological adaptation to lower protein nitrogen turnover, catabolism, and nitrogenous waste load [122] . The lower T3 levels and accompanying difficulties without rT3, reduced free T4 levels, raised TSH, and hypo responsiveness of TSH to TRH contradict the "euthyroid" status and suggest that thyroid supplementation may help CKD[121, 122]. Thyroid hormone supplementation in CKD has not been established after 30 years of research. T3 replacement generally causes muscle catabolism and negative nitrogen balance, indicating that CKD patients should not repair their low T3 levels. Whilst hypothyroidism is clearly dangerous, the threshold for thyroxine supplementation in CKD remains unclear [97, 98] . Mild TSH increases (less than 20 IU/ml) without low T3/T4 do not require thyroid hormone treatment. Before choosing a treatment, one must weigh the risks of hyperthyroidism, the teleological benefits of hypothyroidism in CKD, and the lack of evidence supporting thyroid hormone replacement [103] . After carefully assessing the clinical aspects, possible hypothyroid symptoms, advantages, and dangers of thyroid hormone therapy or not, treating nephrologists and endocrinologists should make a therapeutic choice for each patient. CKD reduces iodide excretion, which increases serum inorganic iodide, thyroid gland iodine, and thyroid gland

hypertrophy. CKD patients had higher rates of goitre (particularly in women), thyroid nodules, and thyroid cancer than the general population. CKD does not increase autoimmune thyroid disease [104]. CKD patients rarely have positive thyroglobulin and thyroid microsomal antibodies. Autoimmune thyroid disease may occur with other CKD-related autoimmune disorders including lupus nephritis, type 1 diabetes, etc. Antithyroid antibodies should be tested for increased TSH in autoimmune illness. CKD does not affect autoimmune thyroid disease management[111].

**2.7 Extrapulmonary Clinical Manifestations in COVID-19: Thyroid Gland and Kidney**

All ACE2-expressing cells are susceptible to SARS-CoV-2 infection [62, 63]. As previously noted, ACE2 receptors are also highly expressed in the kidneys, heart, liver, gastrointestinal (GI) tract, neuronal cells, and vascular epithelial cells in addition to the lungs [75, 77]. Thus, people with COVID-19 experience symptoms in different organs and systems in addition to the classic respiratory symptoms including severe shortness of breath, laborious and abnormally quick breathing, low blood pressure, and fatigue[1]. A number of nonspecific or unusual extra-pulmonary problems, including as systemic inflammation, hypercoagulability, and renin-angiotensin-aldosterone system (RAAS) dysregulation, are also being experienced by COVID-19 patients [51]. These symptoms frequently put off testing, diagnosis, and the desire to find a good treatment. The frequency of COVID-19 rises with age and the existence of pre-existing disorders, despite the fact that the pathogenesis of these problems is not fully understood [5, 14]. In-depth knowledge of the vast array of peculiar extra-pulmonary manifestations of COVID-19 could enhance disease

surveillance, halt transmission, and, most importantly, minimize consequences affecting numerous organ systems, such as the endocrine glands (thyroid) and kidney.

### 2.7.1 COVID-19's Effect on the Thyroid Gland

It is known that the thyroid gland and viral infection interact intricately through hormones and immunomodulatory signaling molecules [62] . These links have been proven in pathological and physiological contexts. Viruses and the inflammatory-immune reactions they cause may be considered a significant factor that might alter thyroid function throughout one's life, helping to define one's unique "thyroid biography"[62, 63,120].

By both genetic and nongenomic pathways, thyroid hormones regulate both innate and adaptive immune responses. L-thyroxine (T4 and 3,3',5-triiodo-L-thyroxine) physiological quantities induce the generation and release of cytokines, which are also elements of the "cytokine storm" that may characterize systemic viral infections [120] . Moreover, thyroid hormones can enhance interferon (IFN) antiviral effects. As an additional point of interest, thyroid disorders such as classical autoimmune thyroid diseases (AITD), interferon-related thyroid disease, immune checkpoint inhibitor mediated thyroiditis, and alemtuzumab-induced thyroid dysfunctions exhibit some immune pathways (such as the hyperactivation of Th1 helper cells responses) of virus infection [62 ,63] . Yet, clinicians are well-versed in the data that infection can be recognized as an environmental stimulant precluding or speeding the development of AITD and the etiology of subacute thyroiditis [112] . However, in patients with decompensated hyperthyroidism, respiratory infections may cause a thyroid storm, which may increase the risk of infection-related mortality due to cardiovascular morbidity. It's also crucial to remember that T4 has been shown to stimulate human platelets, which may contribute to the pathological clotting that occurs as a side

effect of viral infections[115]. The link between COVID-19 and thyroid should be better understood in light of these.

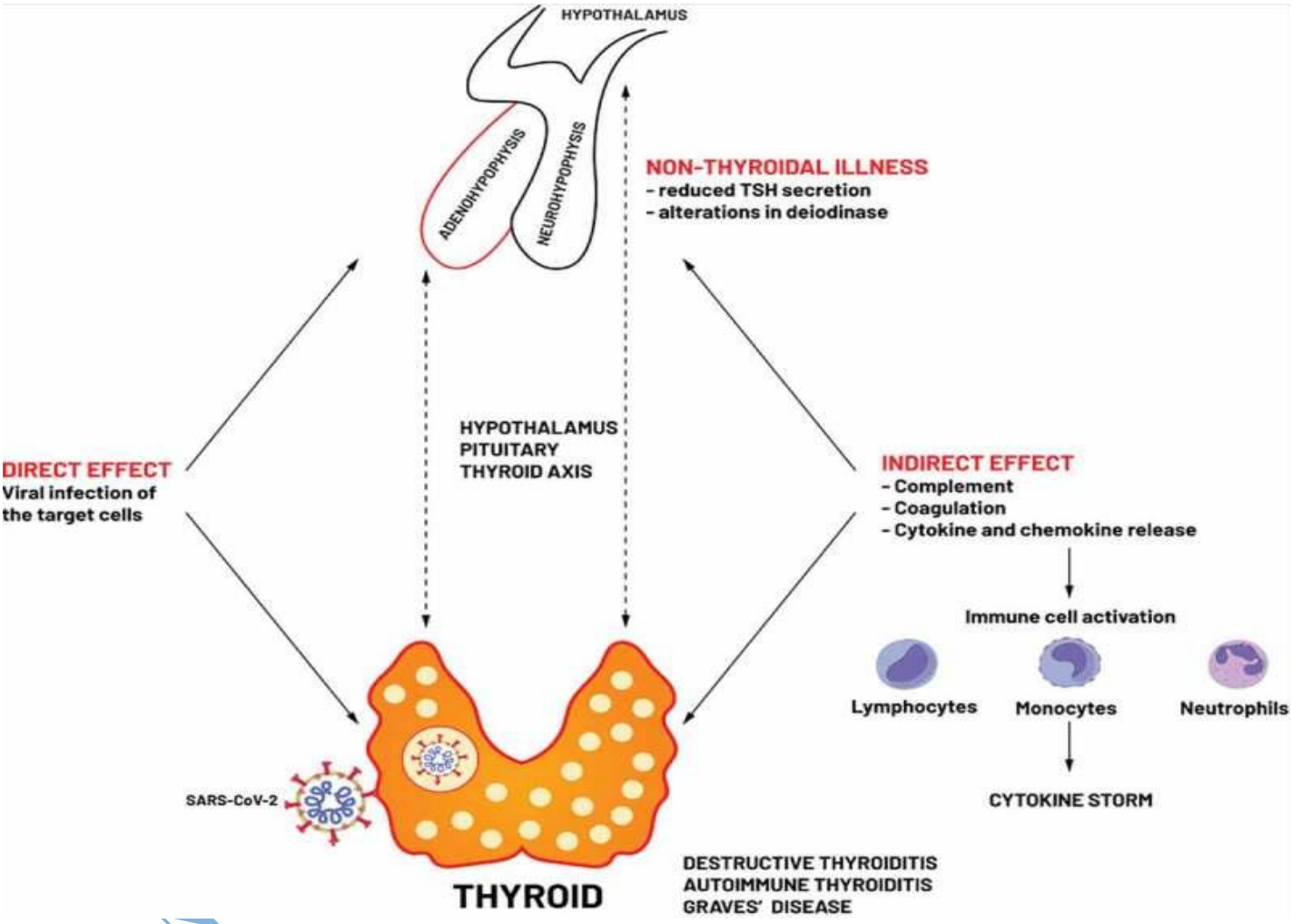


**Fig. 2.6: COVID-19's Effect on the Thyroid Gland[123].**

Source: Medicine (United Kingdom), 2023.

**Thyrotoxicosis**

The release of preformed thyroid hormone as a result of the destruction of the thyroid follicles causes destructive thyrotoxicosis, a very unusual cause of thyrotoxicosis [123] . Many causes of destructive thyroiditis, such as postpartum, sporadic, and drug-induced types, as well as painful subacute thyroiditis (SAT) connected to microbial infection (lithium, amiodarone, interferons, immune-checkpoint inhibitors and so on)[124, 125].

SAT is a self-limiting thyroid inflammatory condition that is considered to be brought on by viruses[124, 125]. Human leukocyte antigen (HLA) haplotype appears to play a significant role in the development of SAT, conferring susceptibility to the condition that primarily affects women [126]. The acute onset of SAT may occur during viral outbreaks and is frequently preceded by an upper respiratory tract infection brought on by a virus such as influenza, adenovirus, coxsackie, or less frequently Epstein-Barr and cytomegalovirus [112]. As a result, it can be considered a viral or post-viral manifestation [125]. The clinical course of the SAT typically consists of three parallel phases that take place over the course of around six months [124] . As preformed thyroid hormones are released from the injured gland at the beginning and in the first few weeks, inflammatory destruction of the thyroid causes a temporary condition called thyrotoxicosis [123] . Many patients experience a hypothyroid phase within a few weeks when their thyroid hormone reserves are exhausted. This period, which can last three months or longer, is frequently followed by the restoration of euthyroidism [127] . Beta-blockers may be used to treat the symptoms of transient thyrotoxicosis in more severe cases, however anti-thyroid medications should not be used

because the thyroid gland does not produce excessive amounts of thyroid hormone [125, 126] . Levothyroxine medication should be continued for around 6 to 9 months before being discontinued to check whether thyroid function has returned to normal. Thyroid hormone replacement therapy may be initiated in individuals who are symptomatic during the hypothyroid period or if this phase is prolonged[122]. The self-limiting nature of the illness causes its diagnosis to be frequently underestimated. Nonetheless, the condition shouldn't be disregarded as long-term consequences, such autoimmune hypothyroidism, have been observed and the accompanying thyrotoxicosis may worsen the clinical course of concurrent illnesses[124]. Although preexisting Hashimoto's thyroiditis and high serum levels of thyroid antibodies are most closely linked to persistent hypothyroidism, all kinds of thyroiditis can proceed to permanent hypothyroidism as a result of severe and widespread inflammatory damage to the gland. Those who experience a more severe hypothyroid phase are more prone to experience this outcome [125, 126]. This is the situation, for instance, when severe thyroiditis develops after immunotherapies for cancer[124].

The recent SARS-CoV-2 pandemic has led to the discovery of SAT as a potential endocrine consequence brought on by COVID-19. Following the initial case reports, a retrospective study of 287 COVID-19 hospitalized patients found that thyrotoxicosis was associated with destructive thyroiditis 20.2% of the time [128] . This finding was supported by the condition's self-limiting clinical course in the absence of TSH-receptor autoantibodies (TRAb), as well as by the association with elevated serum IL-6 levels. Indicating a higher risk of SAT during and after SARS-CoV-2 infection, this incidence was higher than would be predicted in the general population[112]. Like this, a study discovered a higher prevalence of thyrotoxicosis caused by SAT in a cohort of 85 COVID-19 patients admitted to high intensity care units (HICUs) when compared to 78 patients admitted to the same HICUs in 2019 who were SARS-CoV-2 negative,

serving as the control group (15% vs 0.5%, P = 0.002) [129] . Pre-existing thyroid conditions, whether autoimmune or not, did not pose a threat to the emergence of SARS-CoV-2-related SAT [130] . On the other hand, two investigations from the UK that included hospitalized patients with varying degrees of COVID-19 severity revealed a low rate of SAT-related thyrotoxicosis[129]. A study including 191 COVID-19 patients (mean age 53.5 17.2 years; 51.8% male), ten patients had isolated low TSH, suggesting subclinical thyrotoxicosis caused by thyroiditis, although the contribution of autoimmunity was likely in two of them. In contrast, ten patients had isolated low fT3, probably related to NTI [131] . The majority of the 60 COVID-19 hospitalized patients in a subsequent study, which was carried out in an Indian tertiary care teaching hospital, were found to be euthyroid, but 35% of them had one or more abnormalities in their thyroid function, with low TSH being the most common (11 patients or 18.33%); one patient had a typical pattern of thyroiditis [132] . No conclusive link between the severity of COVID-19 and thyroid function tests (TFTs) was found. It was then concluded that even in the absence of underlying thyroid disorders, modifications of TFTs could occur after COVID-19 infection, with thyroiditis and NTI combining to cause the most common alteration. Unfortunately, there was very limited data available in both investigations regarding the clinical characteristics and treatment of patients with TFT changes. A different study by the majority of COVID-19 patients (86.6%) were euthyroid, with no cases of thyrotoxicosis being noted [133] . NTI was the most frequent thyroid function abnormality noted in both and a prior retrospective investigation. COVID-19 patients exhibited lower TSH and FT3 levels than those without COVID-19 [112] . In a similar manner, in a single-center study involving 144 COVID-19 patients, 50% of them had normal thyroid function tests both at the time of admission and at the follow-up, while 39% of patients were found to have low TSH levels at the time of admission or while they were in the hospital, which was associated with low FT3 in 50% of them. In this series, NIT was more likely to blame for the low

TSH reading than destructive thyroiditis[134]. HICU patients compared to non-HICU hospitalized patients, patient settings, and/or confounding variables such medications or iodine-containing contrast agents may all contribute to this variation in the occurrence of SAT across studies. To more accurately assess the prevalence of thyrotoxicosis associated with SAT during COVID-19, large epidemiological multicenter investigations are required.

**Hypothyroidism**

Several investigations have noted cases of primary hypothyroidism linked to COVID-19. In a study, 5.2% (15/ 287) of patients experienced primary hypothyroidism, which was subclinical in 90% of instances (FT3 and FT4 within reference limits) and overt in the remaining 10%[135]. Also, the authors discovered that the in-hospital death rate for COVID-19 patients with hypothyroidism was higher than it was for COVID-19 patients with euthyroidism [135] . Hypothyroidism may thus have a detrimental effect on the results of COVID-19, similar to thyrotoxicosis but perhaps to a lower level. A report of individuals with COVID-19 admitted to high intensity care units had two additional episodes of primary hypothyroidism caused by chronic autoimmune thyroiditis (CAT) (HICUs) [129] . It appears that primary hypothyroidism manifested in both of these instances during COVID-19 and persisted after discharge. Seven days following mild COVID-19 resolution, a case report of overt primary hypothyroidism caused by CAT was reported. There is some evidence to suggest that primary hypothyroidism may develop during or after COVID-19 [136].

The biochemical definition of central hypothyroidism is low FT4 with abnormally low/normal TSH. Seldom described are hormonal alterations that are compatible with central hypothyroidism brought on by SARS-CoV-2 damage at the hypothalamus or pituitary level of the HPT axis [137]. Patients hospitalized for non-mild COVID-19 who had low FT4 with low/normal TSH might be

identified with central hypothyroidism in 2-6% (one to three out of 50 patients). The fact that these hormonal changes were reversed upon recovery from COVID-19 supports the possibility that COVID-19 had acute or temporary effects on the HPT axis[138].

**Nonthyroidal Illness Syndrome**

The nonthyroidal illness syndrome (NTIS) is made up of a number of metabolic changes in various TH target organs as well as alterations to the main HPT axis component [139] . Cardiovascular, respiratory, viral, and cancer diseases are only a few of the acute or chronic systemic illnesses that can cause NTIS[140]. Low plasma T3, low or normal plasma T4, or elevated plasma reverse (rT3) in the presence of normal or slightly reduced TSH are the most common hormonal alterations[105]. As opposed to primary or secondary thyroid problems, the "nonthyroidal sickness syndrome" has a different hormonal profile[105, 139]. While the other synonym, "low T3 syndrome," underlines that low T3 is the biochemical signature of this disease, the term "sick euthyroid syndrome" explains the presence of normal TSH readings in the presence of low T3 and occasionally also T4 concentrations[139] . NTIS is believed to be an adaptive and protective condition that conserves energy in a person who is under stress and on a restricted diet of macronutrients in a severe phase of the systemic disease[105]. Instead, NTIS is linked to negative outcomes, usually mortality, throughout the extended phase of critical illness when patients still rely on intense medical care and parental nourishment[141] . Compared to survivors, critically ill patients who pass away have substantially lower plasma levels of T4, T3, and TSH and greater levels of plasma rT3. As they influence a number of genes involved in TH metabolism, cytokines generated during sickness are regarded as a significant factor of NTIS[140, 141].

Hence, it was possible that COVID-19 non-mild instances could cause NTIS. In fact, studies described severe and critical COVID-19 patients with NTIS. it was revealed that at least 30%

(15/50) of hospitalized patients had hormonal changes that may be attributed to NTIS [126]. Moreover, a substantial positive association between the severity of COVID-19 and the TSH and FT3 readings was discovered, just as it had been shown to be the case for SARS [142, 143]. Remarkably, after recovering from COVID-19, these hormonal alterations returned to normal without the use of thyroid replacement therapy [142]. In two investigations, it was discovered that mean TSH and T3 (and FT3) values were lower in patients with COVID-19 pneumonia than in control groups as a result of NTIS or a specific action of SARS-CoV-2 on TSH secreting cells. Nevertheless, glucocorticoids could also be responsible for the observed drop in TSH levels[136].

Finally, it is significant to highlight that TSH and FT3 values were markedly lower in died patients with severe or critical verified COVID19 than in recovered individuals [136]. The latter finding may be a key indicator of the significance of low TSH and FT3 as indicators of poor outcome in COVID-19 patients who are severely ill and in critical condition. Future research should focus on confirming this data and examining how using particular medications affects treatment outcomes in this situation (i.e., hypothalamic releasing factors, triiodothyronine, thyroid hormone analogues).

### 2.7.2 Autoimmune Thyroid Disorders and COVID-19

The development of an autoimmune disease that may last for a very long time after the acute viral infection has cleared up in a subgroup of patients is one of the most intriguing potential clinical outcomes of SARS-CoV-2 [33]. Following SARS-CoV-2 infection, patients have been reported to experience autoimmune sequelae such as antiphospholipid syndrome, autoimmune thrombocythemia, hemolytic anemia, and Guillain-Barré [45]. Moreover, latent autoimmunity was examined by comparing the levels of a panel of rheumatoid, thyroid, and phospholipid autoantibodies in sera samples from 120 hospitalized COVID-19 patients to pre-pandemic

samples from 100 healthy people. Patients with COVID-19 showed latent autoimmunity, which was mediated by a greater frequency of autoantibodies such TPOAb, rheumatoid factor (RF), and antinuclear antibodies (ANAs), to name a few, compared to controls. The most prevalent autoantibodies in COVID-19 patients were RF and ANA, according to a meta-analysis of a few studies that supported the higher prevalence of these antibodies. These results support future post-COVID research to assess the emergence of overt autoimmunity and point to a role for SARS-CoV-2 infection in promoting/amplifying autoimmune diseases (AIDs)[144].

The same molecular mechanisms that cause severe viral infection to induce autoimmunity also may increase the likelihood that AITDs will develop in COVID-19 patients: molecular mimicry, viral and bacterial superantigens that change the T cell repertoire, and lymphocyte apoptosis followed by an increase in autoreactive lymphocytes [136, 144]. A putative molecular resemblance between COVID-19 viral proteins and human tissues antigens has been demonstrated recently[145]. They showed that thyroid tissue, among other human tissues, was reactive to SARS-CoV-2 antibodies. They demonstrated similarity and homology between spike, nucleoprotein, and numerous other SARS-CoV-2 proteins and the thyroid tissue antigen TPO, among others, using selective epitope mapping [146]. Throughout the course of COVID-19, the broad immunological cross-reactivity between SARS-CoV-2 antibodies and several antigen groups may help to hasten the establishment of autoimmunity in vulnerable subgroups and may even exacerbate autoimmune in people who already have AIDs [145, 147]. The existence of so-called superantigens within SARS-CoV-2 is another intriguing mechanism put forth for AID induction. These superantigens stimulate excessive adaptive immune system activation and cause nonspecific T-cell expansion by directly binding to T cell receptors (TCR), as well as expansion of plasmablasts, which may produce autoreactive IgG [145, 146, 147]. In children who developed a rare secondary inflammatory syndrome, now known as multisystem inflammatory syndrome in

children (MIS-C), after severe COVID-19, the expansion of a population of T-cells with a skewed TCR repertoire consistent with superantigen activation as well as an increased number of proliferating plasmablasts appeared to correlate with elevated pro-inflammatory cytokines associated with cytokine storm [144] . Large intact viral molecules, particularly spike proteins produced from SARS-CoV-2, are thought to be able to enter the lamina propria through a zonulin-dependent increase in mucosal permeability, functioning as superantigens and causing a cytokine storm and autoimmune [133] . In this context, the crucial function of type 1 IFN in regulating viral load has been stressed. Based on the effects of significant lymphopenia during acute infection, another theory for the emergence of post-COVID-19 autoimmunity has been proposed. As lymphocytes die, there may be a brief loss of self-tolerance due to immunosuppression (both of innate and acquired immunity), which is followed by a skewed repertoire expansion and normalization of lymphocytes once the infection is under control[148, 149]. The growth of autoreactive cells and the development of autoimmune diseases may result from both this temporary immunosuppression and an ineffective method of immune reconstitution in susceptible people[149]. Finally, as previously mentioned, intriguing similarities between COVID-19 immune responses and autoimmune illnesses, especially thyroid problems, have been discovered. Nonetheless, there is still a dearth of evidence that COVID-19 and thyroid autoimmunity are related. Even in patients with minimal symptoms, autoimmune thyroid disorders (AITDs) have been labeled as COVID-19 comorbidities[148]. A study documented a case of postpartum thyroiditis (PPT) in a young lady who has already been diagnosed with HT, whereas and corroborated by a case of Hashimoto's thyroiditis (HT) during COVID-19 [150] . The two case reports are highly descriptive and do not allow for the establishment of a causal link between SARS-COV-2 infection and the emergence of AITD, especially in light of the fact that

HT is a significant risk factor for the emergence of PPT later on. So, it is still unclear whether the viral infection is an epiphenomenon or an autoimmunity-causing factor.

Two cases of autoimmune hyperthyroidism (Graves' disease) have been identified following SARS-CoV-2 infection. A 60-year-old woman who had Graves' illness at age 23 and had been in remission since she was 25 was one of the two patients. She had an autoimmune hyperthyroidism recurrence one month following the clinical beginning of COVID-19, necessitating medical attention. One month following the commencement of COVID-19, the other patient, a 53-year-old woman, was diagnosed with newly-onset Graves' illness [151]. Study supported the aforementioned reports which two additional cases of relapse of GD after SARS-CoV-2 infection in two women, aged 45 and 61 years, respectively, who have already been diagnosed with GD and had maintained a normal thyroid function for about 4 years prior to contracting SARS-CoV-2 infection, a similar case of de-novo occurrence of GD following mild symptomatic COVID-19 was reported in a 21-year-old woman [152]. Lastly, a 45-year-old white lady with a history of Graves' disease who has been in stable remission for more than four years has recently been diagnosed with a thyroid storm that was likely triggered by COVID-19 infection. The nasopharyngeal swab of the patient, who had reported the onset of respiratory symptoms more than a month earlier, remained positive at the time of the thyrotoxic crisis. The chronological sequence indicates that GD may have been brought on by SARS-CoV-2 infection in all of the patients. A common environmental trigger implicated in the pathophysiology of autoimmune thyroid disorders is viral infections [151]. Additionally, it has been observed in other autoimmune disorders, the hyperactivation of the immune system and the hyperinflammatory state brought on by SARS-CoV-2 infection may have set off an immunological cascade that resulted in the development or reactivation of thyroid autoimmunity in individuals with a genetic predisposition.

The GD recurrence during COVID-19 may have also been caused by other possible factors, such as stress[153].

In light of this, patients with pre-existing autoimmune diseases should be at risk for experiencing a relapse of the disorder (for example, recurrence of hyperthyroidism and/or thyroid storm in Graves' disease patients) or new onset of the related disorder (the development of PPT in the woman with Hashimoto's thyroiditis after SARS-CoV-2 infectious) and vigilant thyroid function monitoring should be advised, to prevent missing the diagnosis and delaying treatment[154]. On the other hand, autoimmune conditions that already exist do not appear to increase or decrease the likelihood of obtaining COVID-19 or SARS-CoV-2 infections, respectively. The overall course of the COVID-19 disease is not much worse in patients with a preexisting autoimmune inflammatory disease, whether thyroidal or not, contrary to what was first believed, according to findings from current literature [146] . Future prospective research should investigate potential linkages and connections between SARS-CoV-2 and thyroid autoimmunity, as well as how they might affect the emergence of overt autoimmune.

### 2.7.3 SARS-CoV-2 Infection and the Kidney

Recent autopsy analysis on six COVID-19 patients revealed that all renal specimens had various degrees of acute tubular necrosis. All the samples' kidney tissues contained SARS-CoV-2 nucleoprotein (NP) antigens and NP positive inclusion bodies. Moreover, a transmission electronic microscope revealed the presence of virus-like particles in kidney tissues [155] . In 26 autopsies of COVID-19 patients, examined kidney showed abnormalities and discovered extensive proximal tubular destruction with the removal of brush boundary [156] . Subsequent research revealed that diffuse necrosis is visible under a light microscope, and coronavirus particle clusters with characteristic spikes were visible in the tubular epithelium and podocytes

under electron microscopy. SARS-CoV-2 NP antigens and RNA were reportedly found in the urine of COVID-19 patients[157]. These findings and the discovery of SARS-CoV-2 invasion in the kidney are consistent. SARS-CoV-2 as a whole has the potential to directly infect human renal tubules and cause kidney injury[157].

According to recent research, COVID-19 patients had an acute kidney injury (AKI) incidence that ranged from 0.5% to 28.5%, and they also had a higher frequency of renal function damage when their blood urea nitrogen (BUN) or serum creatinine (Scr) levels were raised[158]. According to a research of 193 COVID-19 patients, levels of BUN and Scr were elevated in 27 (14.0%) and 20 (10.4%) of the patients, respectively, with COVID-19. 129 individuals had routine urine tests done, and 76 (58.9%) of them tested positive for urinary protein, while 57 (44.2%) tested positive for hematuria[159]. Another study revealed that 14% of COVID-19 patients had impaired renal function [160] . Moreover, AKI rates are higher in COVID-19 individuals whose disease is progressing more rapidly. The result of a study also revealed that none of the 28 patients who did not need care in the ICU had AKI, while three (23.1%) of the 13 patients with AKI in the ICU were observed[161]. COVID-19 patients with AKI had a clearly greater death rate than COVID-19 patients without renal damage. In addition, more severe patients had higher rates of AKI in a different study looking at 193 patients with COVID-19 at hospital admission, and the Cox regression analysis also revealed that COVID-19 patients who had AKI had a considerably greater death risk. As a result, AKI is more common in severe COVID-19 cases [162].

Many studies have revealed that kidney dysfunction (elevated blood urea nitrogen [BUN] and SCr), abnormal urine analyses (proteinuria and hematuria), and radiographic abnormalities of the kidneys are the main symptoms of renal functional impairment[163]. Proteinuria, which is present in more than half of patients before or after admission, is the most frequent clinical manifestation,

followed by hematuria, increased BUN, and raised SCr (33.7, 14.3, and 10.7%, respectively)[161]. Also, a meta-analysis showed that patients had albuminuria in varied degrees (+ in 38.8% of the patients and ++ or +++ in 10.6% of the patients). AKI has been shown to be a significant risk factor for mortality during SARS-CoV-2 infection, particularly in severely ill individuals. After being hospitalized, 33.9% of patients with SARS-CoV-2 infection and AKI were reported deceased, and this rate was substantially greater than that of patients without renal damage (p 0.001)[163, 164]. Furthermore, renal parenchymal inflammation and edema, detected by a CT scan, are equally common[164].

It was discovered that the renal impairment was more obvious the more severe the SARS-CoV-2 infection was. Although they were used to assess renal function, the blood BUN and SCr tests were not sensitive enough to detect early kidney impairment[164]. Urine microprotein, urine IgG, and urine transferrin were found to be sensitive markers of early glomerular injury, while urine 1-microglobulin could signify early renal tubular damage. Infected patients may benefit from early renal damage detection using the estimated glomerular filtration rate, Cystatin C, and urine microalbumin/creatinine ratio calculations NGA[164].



**Potential Mechanisms of Renal Injury**

Several investigations suggested that SARS-CoV-2 infection and virus-induced cytokines such IL-6 and IL-10 were responsible for kidney damage in individuals with SARS-CoV-2 infection, however these explanations are insufficient. Many mechanisms may contribute to renal impairment. The potential mechanisms of renal damage are outlined here[165].

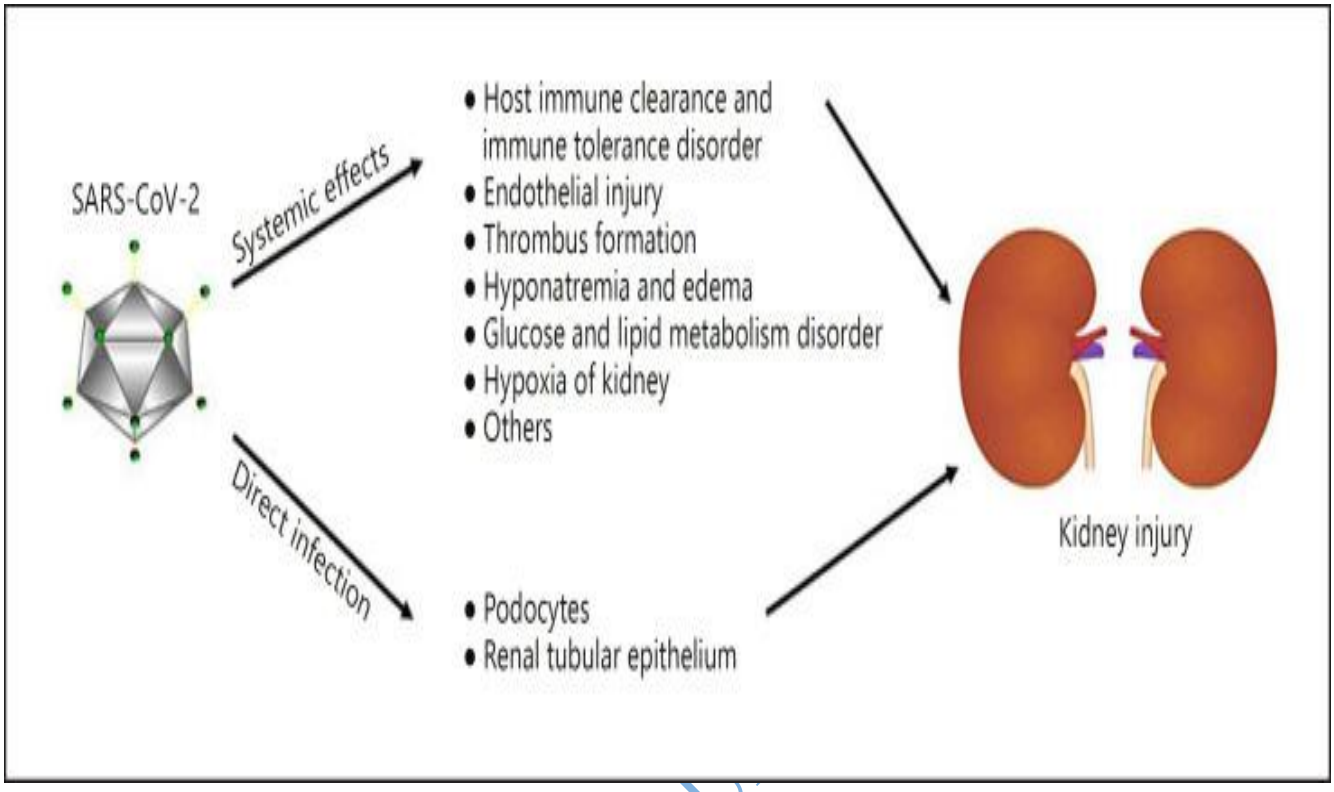


**Fig. 2.7: COVID-19's Effect on the Kidney**[165].

Source: Infection Kidney Dis, 2021

**Direct Renal Infection by SARS-CoV-2**

Available evidence at hand indicates that SARS-CoV-2 binds to ACE2 via the S1 subunit and directly damages intrinsic renal cells. The kidneys and bladder are enriched with ACE2, making the renal tissue susceptible to SARS-CoV-2, according to single-cell RNA sequencing data from human tissue and ACE2 labelling[166, 167]. The presence of coronavirus-like particle clusters in the renal tubular epithelium and podocytes and the ability to observe specific SARS-CoV-2 nucleoproteins in a nuclear or cytoplasmic pattern using indirect fluorescence raise the possibility that the virus could infect renal cells directly. The results of the autopsy revealed that the virus reached the blood and caused viremia after infecting the respiratory tract[168]. As a result, they deduce that the virus may enter the urinary system via blood flow, bind to and internalize with ACE2 receptors, and infect kidney cells that express the ACE2 receptor, such as renal tubular epithelial cells, podocytes, and others. The widespread kidney damage, however, cannot entirely be attributed to the low and unevenly distributed viral load in the kidneys, according to recent studies[169].

**Systemic Effects of SARS-CoV-2 Infection on the Kidneys**

The balance between viral eradication and immune system toleration determines the severity of SARS-COV-2 infection. Viral injury to the body may be caused by immune clearance abnormalities as well as immunological resistance to infections[169, 170].

The detection and removal of coronaviruses, as well as the activation of the inflammatory signaling pathways downstream, are carried out by macrophages. The cellular adaptive immune response is then launched. Helper T (Th) cells can be made to differentiate into Th1 and Th2 cells, the former of which can activate cytotoxic T cells that, like natural killer (NK) cells,

destroy virus-infected cells. Th2 cells then work with B lymphocytes to produce antibodies that stop viral replication [166] . Following SARS-CoV-2 invasion, this is the immunological clearing process of anti-infection, which is accompanied by the creation and release of several inflammatory cytokines. These cytokines support the innate and adaptive immune response by taking part in the body's antiviral activities[166, 168].

An immune clearance dysfunction prevents the virus from being recognized and eliminated, leading to an infectious spread. Massive viral replication may cause immune cells to respond excessively, which could result in a significant inflammatory response and clinical signs. Dendritic cell, monocyte, and T-cell responses are shown to be widely reduced during the acute phase of SARS-CoV-2 infection, which supports a weakening of immune response initiation and viral clearance [169,170] . A high level of inflammatory cytokines is produced as a result of the activation of the interferon (IFN)-1 signaling pathway and the JAK-STAT signaling pathway, which in turn causes high amounts of viral nucleic acid (RNA) to accumulate in the body as a result of impaired immunological clearance. An autoreactive adaptive immune response may be produced because of the IFN-1 signaling pathway activation, which may exacerbate tissue damage [42, 46] . In addition, the host's inherent resistance to the infection causes an overactive immune response that directly results in numerous organ failures, including kidney, liver, and heart failure. This overactive immune response is caused by cellular immune disorders, cytokine storms, and immune compounds[166].

Normally, CD8+ T cells and NK cells kill virus-infected cells. However, it was discovered that individuals with SARS-CoV-2 infection had lymphopenia predominately caused by CD8+ T-cell depletion, a cellular immunological disease that prevented sufficient cytotoxicity against virus-infected target cells. Moreover, lymphopenia induces an excessive generation of inflammatory

cytokines due to the feedback loop, which severely damages tissues and organs[148, 149]. It has been established that NK cells, which can non-specifically kill virus-infected cells, are substantially activated in acute SARS-CoV-2 infection and express high levels of perforin, NKG2C, and Ksp37 in severe instances. Tissue damage might be caused by an uncontrolled NK-cell response and an overabundance of cytotoxic granules. One of the causes of the observed kidney damage is thought to be a perturbation of the cellular immune system as a whole[99].

A cytokine storm, an immunopathologic condition that can be lethal, results from unchecked cytokine production during the aforementioned immunological response. Infection causes lymphocyte activation, which triggers the release of inflammatory cytokines to kill the infected cells [171] . However, patients may experience severe endothelial dysfunction, disseminated intravascular coagulation, and multiple organ dysfunction syndrome as a result of the excessive cytokine release. According to studies, cytokine expression, such as that of IFN-, interleukin (IL)-6, IL-10, granulocyte colony-stimulating factor, and monocyte-chemotactic protein 3, was higher in SARS-CoV-2 patients than it was in healthy controls[172]. There is a clear inflammatory infiltration of the renal interstitial in the kidneys, which is primarily made up of lymphocytes and plasma cells with a few eosinophils[173]. Additionally, it suggests that activated lymphocytes move towards kidney tissues in order to kill infected renal cells and release inflammatory cytokines, which in turn causes tissue damage and localized inflammation. Moreover, kidney damage is caused by cytotoxic particles such perforin, granulysin, and proinflammatory cytokines, which are strongly expressed in lymphocytes[148, 149].

Immune complex deposition may harm kidneys in addition to cellular immunity and a cytokine storm [174] . The interstitium appears to be the primary site of damage in SARS-CoV-2-infected patients' renal disease, with minimal glomerular abnormalities. Due to ACE2 expression in

podocytes, glomerular lesions such localized segmental glomerulosclerosis and collapsing glomerulopathy are linked to viral infection and mostly present as podocyte-related damage [163]. However, substantial endothelium damage, including edema, foamy alterations, and subcutaneous transmittal enlargement, was also noticed in addition to podocyte damage[55]. While there was no evidence of inflammatory cell infiltration in the glomeruli, direct or indirect immunofluorescence, electron microscopy, and IgG, IgM, and trace C3 were discovered in the granular tissues of the capillary wall, pointing to immune complex deposition as one of the causes of glomerular injury[163]. Immune complex-associated nephritis results from the deposition of immune complexes along glomerular capillaries, and its underlying mechanism may involve immune complexes activating the complement system and causing kidney damage[175].

**Endothelial Cell Injury**

Endothelial damage to the kidney's glomeruli is visible under an electron microscope in the form of cell swelling and foam-like alterations, subendothelial expansion, and endothelial proliferation [176]. Since tubular epithelial cells express a lot of ACE2, it is thought that the virus could connect to them and cause damage to them directly. Many patients in severe condition experience vasculitis-like signs or even gangrene on their extremities as a result of vascular endothelial injury and a cytokine storm [177]. Small vessel hyperplasia, vessel wall thickening, lumen stenosis, occlusion, and localized bleeding are all discovered during pathologic exams. The underlying cause of vascular damage could be vasculitis[178].

**Thrombus Formation**

Many patients with severe SARS-CoV-2 infection present with thrombosis and thrombocytopenia due to hypercoagulability and disseminated intravascular coagulation. Moreover, segmental microthrombi in the glomeruli of SARS-CoV-2 patients were discovered in

two pathological examinations of caducous kidneys [156, 168] . Although the exact mechanism of coagulation is still unknown, studies have shown that endothelium damage increases tissue factors, which then activates external coagulation pathways. The complement system is crucial in speeding platelet adhesion and aggregation, endothelial cell damage, and thrombosis since it is the host immune system's initial response to SARS-CoV-2 infection. Due to substantial coagulation activation, thrombocytopenia, which is frequent in individuals with severe SARS-CoV-2 infection, may potentially be linked to decreased platelet consumption. Large-scale microthrombi development results in kidney injury[178].

**Hyponatremia and Edema**

Several patients during the SARS-CoV-2 virus pandemic suffered inexplicable edema in the lungs and extremities, and other individuals experienced abrupt severe hyponatremia[179, 180]. This shows that these people have a malfunction of the way their bodies process salt and water, which is a major risk factor for AKI. Although the exact mechanism is unknown, it was formerly thought to be connected to RAS dysfunction. Reduced ACE2 expression in SARS-CoV-2 infection causes an increase in Ang II production, which causes tissue edema. Together with the RAS dysfunction, monocytes, and macrophages release IL-6, which causes an electrolyte imbalance and boosts circulatory volume by causing the nonosmotic production of vasopressin[181]. Hyponatremia and IL-6 are adversely correlated, according to a retrospective study, and hyponatremia seems to be linked to more unfavorable outcomes and more severe disease[178].

**Glucose and Lipid Metabolism Disorder**

Coexistence of chronic diseases is a common occurrence among patients, with chronic renal disease, hypertension, diabetes, cardiovascular and cerebrovascular diseases, malignant tumors, and other conditions occurring more frequently [179, 182] . Serious incidents occur at much greater

rates in people with diabetes[183]. Although the exact explanation is unknown, we surmise that it may be linked to the abnormal glucose and lipid metabolism that is a risk factor for kidney injury in these chronic conditions. According to reports, patients with diabetes and hypertension show less tubular ACE2 protein staining than healthy individuals. Membranal ACE2 expression is further decreased during SARS-CoV-2 infection as a result of the virus's adherence to the cell membrane, which could be one reason why people with diabetes and high blood pressure are more likely to suffer kidney damage[184]. Both viral infection and hyperglycemia have detrimental effects on the kidney therefore, studies emphasize the necessity to effectively monitor blood glucose to enhance prognosis in COVID-19-infected patients with glycated hemoglobin testing[185]. A study indicated that patients with severe COVID-19 had somewhat higher HbA1c levels than those with mild COVID-19, but this difference was not statistically significant (P = 0.52). However, it is notable that only two studies with small sample sizes examined the effect of COVID-19 severity on HbA1c, which may influence the outcomes of interest. In addition, HbA1c shows the average blood glucose level during the previous 2–3 months[186, 187, 188]. Hence, the impact of a short-term viral infection on HbA1c levels may not be significant. However, additional studies with high sample sizes are required to confirm their findings.

**Hypoxia of the Kidneys**

SARS-CoV-2 primarily targets the lungs, which may result in hypoxia if ventilation and diffusion are impaired. Hypoxia in the kidneys may be a factor in AKI. By a variety of causes, including the activation of adrenergic neurons and changes in nitric oxide metabolism, hypoxemia lowers renal blood flow. Both severe hypoxia and ischemia can lead to malfunction of the microvasculature. This may influence nearby intrinsic cells and capillaries, widening the hypoxic zones and causing organ failure[175].

**Other Effects**

Patients with SARS-CoV-2 have been documented to experience rhabdomyolysis, and the renal architecture of these individuals contains significant levels of creatine phosphokinase staining, which suggests that rhabdomyolysis may play a role in the development of AKI. In addition, several medications, heart failure, diarrhea, and hypertension can all result in kidney damage in infected patients[175].

## 2.8 Post-Acute Phase Extrapulmonary Organ Infection in Recovered Positive SARS-CoV-2 Patients

More than 1 million COVID-19 patients have so far been clinically cured and released. Yet, numerous COVID-19 patients who had been released tested positive for SARS-CoV-2 once again. 14.5% (38/262) of COVID-19 convalescent patients from Guangdong, China, had their SARS-CoV-2 status re-detected throughout their follow-up period. In a similar vein, data from Brunei Darussalam revealed that 19.8% (21/106) of recovered patients had tested positive again for SARS-CoV-2. RT-PCR studies on anal or nasopharyngeal swabs validated the re-detectable positive cases. According to these investigations, some individuals who have recovered could still be viral carriers[51].

Patients with COVID-19 could have lung samples, stools, urine, serum, kidney tubules, and gastrointestinal epithelium tested for the presence of the SARS-CoV-2 virus. However, although throat swabs became negative, the viral RNA in urine and stool samples continued to be positive, and the viral RNA can linger in feces for up to 30 days [1, 174, 189]. Using tissue sections from the lung, liver, heart, intestine, and skin of a COVID-19 patient who was ready for release but passed away from cardiac arrest, a study used digital PCR to identify the SARS-CoV-2 [168]. The patient tested positive for SARS-CoV-2 in the cells and tissues of the lung, and the findings show that

SARS-CoV-2 is still present in the lung of the COVID-19 patient who has been released [190] . Moreover, a study showed for the first time that SARS-CoV-2 viral clearance is delayed in male individuals, and they hypothesized that testicular viral reservoirs may have a significant impact on viral persistence in males. SARS-CoV-2 appeared to be kept in the lung or extrapulmonary organs, which may be the cause of the virus testing positive again in patients who had been released[190, 191].

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# Chapter Three

# Methodology

## 3.1 Research Design

This was a cross-sectional study comprising a total of 270 apparently healthy participants (males and females) in the age range 18-60 years at different local government areas in Ibadan, Oyo State. They were recruited for the study after informed consent had been obtained from them. Prior to these, ethical approvals have been obtained from the ethical committee of the Oyo State institutional review board. The study involved not more than 8 months post exposure to SARS-CoV-2 viral infection compared with a matched cohort of apparently healthy individuals who were not exposed.

## 3.2 Study Area

This study was carried out in Ibadan, Oyo state at four different Local Government Areas, which are, Ibadan North, Lagelu, Oluyole and Ibadan Northwest Local Government Area. Apparently healthy exposed and unexposed individuals were recruited for the study.

## 3.3 Population of the Study

The participants were made up of an initial 120 SARS-COV-2 exposed individuals and a matched cohort of 150 apparently healthy individuals without exposure to SARS-COV-2 infection. The population was further screened by analysis of SARS-COV-2 antibody to ensure true exposure and non-exposure. 85 unexposed, those who tested negative to SARS-COV-2 virus, who also tested negative to SARS-COV-2 antibody and 80 exposed who tested positive to SARS-COV-2 viral infection and equally tested positive to the SARS-COV-2 antibody were

involved in the final study. After the initial screening using blood pressure, HBA1C, urea, creatinine and SARS-COV-2 antibody, the final study population was screened down to:

- The exposed individuals --- 80
- The unexposed individuals --- 85

### 3.4 Sample and Sampling Techniques

The formula for sample size calculation for descriptive cross- sectional study is:

$$N = \frac{Z^2pq}{d^2}$$

Where:

Zα = standard normal deviate corresponding to 2-sided level of significance at 5% = 1.96

P = prevalence of kidney injury

q = 1- prevalence

d= level of precision at 5% = 0.05

The prevalence of SARS-CoV-2 in Nigeria is 5.6% in Nigeria (**source**).

P = 5.6% = 0.056

N = Number of participants needed

q= 1- 0.056 = 0.94

$$N = \frac{(1.96)^2 \times 0.056 \times 0.94}{(0.05)^2} = 80.88$$

Therefore, the minimum sample size required is 81[1].

**3.5 Sampling Strategy:** Convenience sampling strategy was employed during this research

### 3.6 Selection Criteria

**3.6.1** Exclusion Criteria for Non-exposed (Control)

- Refusal to give consent.
- Individuals with a history of renal dysfunction, high blood pressure, diabetes, and thyroid disease.
- Presence of COVID-19 antibodies

3.6.2 Exclusion Criteria for exposed (Cases)

- Refusal to give consent.
- Individuals with a history of renal dysfunction, high blood pressure, diabetes and thyroid disease.
- Absence of COVID-19 antibodies

3.6.3 Inclusion Criteria for Non-exposed (Control)

- Apparently healthy individuals 18-60 years, who tested negative for SARS-CoV-2 infection and were not vaccinated.

3.6.4 Inclusion Criteria for exposed (Case)

- Apparently healthy individuals 18-60 years, who tested positive for SARS-CoV-2 infection and were not vaccinated.

### 3.7 Method of Data Collection

#### 3.7.1 Demographic Indices

A semi structured pre-test questionnaire was given to the prospective participants to obtain their qualitative data about the age, gender, background, socio- economic status and the dietary lifestyle of the participants.

#### 3.7.2 Anthropometric Characteristics:

Anthropometric measurements like weight, height, body mass index, waist and hip circumferences and waist/hip ratio) were obtained from the participants.

**Weight:**

The weight of the participants was obtained following the basic/standard method. It was done with a bathroom scale placed on a flat surface. The participants wore light clothing and took off his/her their shoes before standing on the scale. The scale was adjusted to zero before each reading and readings were recorded to the nearest $0.5kg^2$.

**Height:**

The height of participants was measured in centimeters. The subject was asked to stand bare footed uprightly on a hard level ground against a vertical wall and without raising the heels from the ground with the feet kept together while the back and heel were aligned with a ruled bar against the vertical surface. The measurements were made by moving a slide headpiece to the vertex of the subject's head and the reading at that point was recorded to the nearest 0.1meter.

**Body Mass Index (BMI):**

This was calculated using the body weight and height of the subjects. The formula below was used in the calculation[3].

$$BMI = \frac{\text{weight (kg)}}{\text{height}^2\ (m^2)}$$

### 3.8 Blood Sample Collection

An approximate 10mls of venous blood sample was obtained from the participant by venipuncture. This was done by applying a tourniquet 4-6 inches (10- 15cm) above the intended puncture site (preferably cubital vein in the antecubital fossa to obstruct the return of venous blood to the heart and to distend the vein. The site was then cleansed with alcohol swab. 10mls of blood was collected with new disposable pyrogen free needles and syringes after the skin had been air dried and the blood dispensed into plain serum tubes and kept for 1-2 hours to clot[4]. Serum obtained was used for Electrolyte, Urea, Creatinine, Cys-C, TSH, FT4, FT3, C-reactive proteins and SARS-CoV-2 spike protein antibody. Samples were also collected into EDTA bottles for the analysis of HBA1C.

### 3.8 1 Laboratory Analyses

The following biochemical indices are analyzed: Electrolyte, Urea, Creatinine, Cys-C, TSH, FT4, FT3, C-reactive proteins and SARS-CoV-2 spike protein antibody.

### 3.8.2 Determination of Biochemical Parameters

### 3.8.3 COVID-19 Antibodies Estimation

**SARS-CoV-2 IgG II Assay**

The serum SARS-CoV-2 spike protein antibody was analyzed on Architect I1000 (Abbot) auto-analyzer using chemiluminescence immunoassay method. The standardized protocol provided with the Architect I1000 (Abbot) analyzer insert was followed for estimation[5].

**Principle of assay**

Using chemiluminescent microparticle immunoassay (CMIA) technology, this assay is an automated, two-step immunoassay for the qualitative and semi-quantitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma. Sample, paramagnetic microparticles coated with SARS-CoV-2 antigen, and assay diluent are mixed and incubated. Anti-SARS-CoV-2 IgG antibodies found in the sample bind to SARS-CoV-2 antigen-coated microparticles. The combination is washed. Anti-human IgG acridinium-labeled conjugate is added to a reaction mixture, which is then incubated. The Pre-Trigger and Trigger Solutions are added after a wash cycle. As a relative light unit, the ensuing chemiluminescent response is quantified (RLU). There is a direct correlation between the quantity of IgG antibodies against SARS-CoV-2 in a sample and the RLU observed by the system optics[5].

### 3.8.4 Determination of HBA1C

The glycated hemoglobin concentration was carried out on Architect c4000 (Abbot) analyzer using spectrophotometry method. The standardized protocol provided with the Architect c4000 (Abbot) HBA1C insert was followed for estimation.

**Principle of assay**

In HbA1c assay, whole blood samples are lysed in order to release hemoglobin and HbA1c analyte. The lysed sample is introduced to the glass fiber matrix that was previously treated with Blocking Buffer. The binding process between the analyte and the Blocking Buffer binds Hemoglobin and HbA1c to the glass fiber matrix. HbA1c is quantified by determining the amount of HbA1c analyte trapped on the matrix cell utilizing a conjugate of Anti-HbA1c and Alkaline Phosphatase as the signal-generating molecule and 4-Methylumbelliferyl Phosphate as the substrate (MUP) [6].

### 3.8.5 Determination of Cystatin-C

The serum Cyctatin C was analyzed on Cobas C-311 on Hitachi-Roche chemistry analyzer using spectrophotometric method. The standardized protocol provided with the Hitachi-Roche Cobas analyzer insert for cystatin c was followed for estimation[7].

**Principle of assay**

Human plasma is combined with cystatin C immunoparticles. Cystatin C from the sample and anti-cystatin C from the immunoparticles form a complex. The complex particles absorb light, and turbidimetry relates the light absorption to the concentration of cystatin C by interpolation on a standard calibration curve[7].

### 3.8.6 Electrolytes Estimation

The electrolytes sodium, potassium, bicarbonate, and chloride were estimated using Erba Lyte analyzer. For estimation, the standardized protocol included with the ERBA kit was used.

**Principle of assay**

**Ion Selective Electrode ($Na^+$, $K^+$, $CL^-$)**

Ion Selective Electrode (ISE) technology is a type of electrochemical sensor used to measure the concentration of ions in a solution. The ISE consists of a sensitive membrane, which is in contact with the sample and responds to changes in the concentration of certain ions in the sample. On the other side of the membrane is an internal filling solution, and a silver rod acts as an internal electrode, which converts the ionic conduction to electronic conduction. The relationship between ion activity and electric potential conforms to the NERNST equation, which states that the logarithm of the ion activity has a linear relation with the electrode potential. Different electrodes are sensitive to different ions. For example, a sodium electrode is only sensitive to Na ions, and a potassium electrode is only sensitive to K ions. If a potassium electrode, sodium electrode, and chloride electrode are combined, then K ions, Na ions, and chloride ions in the sample can be measured at the same time. In addition to the sensitive membrane, the ISE also consists of a reference electrode, which provides a reference potential and forms a complete measuring circuit. Inside the reference electrode, there is also an internal electrode, whose potential remains constant when the concentration of the solution changes. Thus, it provides a reference point to measure the potential differences[8].

**Manometric method ($HCO3^-$)**

In this process, a certain quantity of blood serum and reagent (lactic acid) are added to a sealed reaction chamber. The reaction chamber is equipped with a pressure sensor that detects changes in gas pressure resulting from the reaction between the $HCO3^-$ ions in the serum and the lactic

acid reagent. As the $HCO3^-$ ions react and release $CO_2$, the gas pressure inside the chamber increases accordingly. The pressure sensor sends the signal to the microprocessor, which calculates the amount of $HCO3^-$ ion present in the sample based on the change in pressure. The result is then displayed and printed out for further analysis. This process is used to determine the AB (Actual bicarbonate) parameter for $HCO3^-$ ion in the blood serum[9].

### 3.8.7 Determination of Urea and Creatinine

The serum Urea and Creatinine was assayed on Architect c4000 (Abbot) analyzer using spectrophotometry method. The standardized protocols provided with the Architect c4000 (Abbot) analyzer insert for urea and creatinine were followed for estimation.

**Creatinine assay principle**

**Methodology: Jaffes Alkaline method**

The creatinine in the sample combines with picrate at an alkaline pH to generate a creatinine-picrate complex. Due to the development of this complex, the rate of increase in absorbance at 500 nm is exactly proportional to the concentration of creatinine in the sample.

**Urea assay principle**

**Methodology: Urease**

The Urea Nitrogen test is a variation of a completely enzymatic technique initially described by Talke and Schubert. 1 The test is a kinetic assay in which the starting rate of the reaction is linear for a specified time period. Urease hydrolyzes the urea in the sample into ammonia and carbon dioxide. The second process, mediated by glutamate dehydrogenase (GLD), transforms ammonia and -ketoglutarate to glutamate and water, while simultaneously oxidizing reduced nicotinamide adenine dinucleotide (NADH) to nicotinamide adenine dinucleotide (NAD). For every molecule

of urea, two molecules of NADH are oxidized. The initial rate of absorbance decline at 340 nm is related to the sample's urea content[10].

### 3.8.8 Determination of C-Reactive Protein

The serum CRP estimation was carried out on Architect c4000 (Abbot) analyzer using spectrophotometry method. The standardized protocol provided with the Architect c4000 (Abbot) analyzer insert for CRP was adhered to.

**Principle of assay**

C-Reactive Protein is an in vitro diagnostic assay used to quantify CRP levels in human serum and plasma. Agglutination is the outcome of an antigen-antibody response between CRP in a sample and polyclonal anti-C-reactive protein antibody that has been adsorbed to latex particles. This agglutination is detected as a change in absorbance, the extent of which is proportional to the amount of CRP in the sample. The actual concentration is then calculated using interpolation of a calibration curve constructed from calibrators of known concentration. Increase in 572 nm absorbance is related to CRP concentration[11].

### 3.8.9 Determination of FT4, FT3, and TSH

The serum TSH, FT4, FT3 estimation were carried out on Architect I1000 (Abbot) analyzer using spectrophotometry method. The standardized protocols provided with Architect I1000 (Abbot) analyzer insert were followed for estimation.

**FT4 assay**

**Principle of assay**

The ARCHITECT Free T4 assay is a two-step immunoassay designed to detect the presence of free thyroxine (Free T4) in human serum and plasma using Chemiluminescent Microparticle

Immunoassay (CMIA) technology with flexible assay protocols, also known as Chemiflex. In the initial step, sample and paramagnetic microparticles coated with anti-T4 are mixed. Anti-T4-coated microparticles bind free T4 (unbound) in the sample. In the second step, T3 acridinium-labeled conjugate is applied after washing. The ensuing chemiluminescent reaction is measured in relative light units after adding Pre-Trigger and Trigger Solutions to the reaction mixture (RLUs). The amount of Free T4 in the sample is inversely proportional to the RLUs identified by the ARCHITECT I optical system[12].

**FT3 assay**

**Principle of Assay**

The ARCHITECT Free T3 assay is a two-step immunoassay that measures the presence of free (unbound) T3 in human serum and plasma utilizing Chemiluminescent Microparticle Immunoassay (CMIA) technology with customizable assay methods, also known as Chemiflex. In the initial step, sample and paramagnetic microparticles coated with anti-T3 are mixed. Anti-T3-coated microparticles bind free T3 (unbound) in the sample. In the second step, T3 acridinium-labeled conjugate is applied after washing. The ensuing chemiluminescent reaction is measured in relative light units after adding Pre-Trigger and Trigger Solutions to the reaction mixture (RLUs). The amount of Free T3 in the sample is inversely proportional to the RLUs identified by the ARCHITECT I optical system.

**TSH assay**

**Principle of assay**

The ARCHITECT TSH assay is a two-step immunoassay that detects thyroid stimulating hormone (TSH) in human serum and plasma utilizing Chemiluminescent Microparticle

Immunoassay (CMIA) technology with customizable assay protocols, also known as Chemiflex. In the first step, sample, paramagnetic microparticles coated with anti- TSH antibody, and TSH Assay Diluent are mixed. TSH contained in the sample binds to microparticles coated with anti-TSH antibodies. Anti- TSH acridinium-labeled conjugate is applied after washing in the second stage. The ensuing chemiluminescent reaction is measured in relative light units after adding Pre-Trigger and Trigger Solutions to the reaction mixture (RLUs). There is a direct correlation between the sample's TSH concentration and the RLUs recorded by the ARCHITECT I optical system[13].

### 3.8.10 Data Analysis

Data obtained was analyzed using SPSS 20. Results were presented as mean ± standard deviation for all parameters. Independent student's t-test was used to evaluate significant differences between mean values. All p-values less than 0.05 ($p<0.05$) was considered statistically significant.

## Endnotes


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# Chapter Four

## Results and Discussion of Findings

### 4.1 Demographic Data

A total 270 apparently healthy participants (Male and Female) were recruited for this study. The age range of the respondents was between 18-60 years. 150 respondents (who tested negative to SARS COV-2 virus within a period of 8 months) were initially recruited as the unexposed, while the remaining 120 participants (who tested positive to SARS COV-2 virus) were recruited as the exposed as demonstrated as seen in the figure 4.1.

# 270 TOTAL PARTICIPANTS


**Figure 4.1: Distribution of Participants into Unexposed and Exposed.**

Source: Author's Field Work, 2023

The 150 unexposed participants were further screened down to 85, excluding those who with high blood pressure, those with urea values greater than 45mg/L, creatinine values greater than 1.5mg/dl, glycosylated haemoglobin greater than 6.4% and those with positive SARS COV-2 virus using RT-PCR method which could compromise the results. Out of the 85 unexposed used for this research, 58 (68.2%) were male while, 27 (31.8%) were female. The age group for the unexposed participants as seen in Table 4.1 below is age 19-25years 18 (21.18%), 25-40years 52 (51.18%) and age group above 40 were 15 (17.65%). The age group that makes up the highest for this study is the most active and productive age group (25-40years) with highest rate of mobility but were partially grounded by the lock-down during the pandemic.

The 120 exposed participants were also further screened down to 80, excluding high blood pressure, those with urea values greater than 45mg/L, creatinine values greater than 1.5mg/dl, glycosylated haemoglobin greater than 6.4% and those with negative SARS COV-2 virus using RT-PCR method which could compromise the results. From the 80 exposed group used for this research, 54 (67.5%) were male while, 26 (32.5%) were female. The age group for the exposed participant as presented in Table 4.2 below is age 19-25years 19 (23,8%), 25-40years 38 (47,5%) and age group above 40 were 23 (28.8%).

Furthermore, from table 4.1 and 4.2 below, bulk of the participants both in the unexposed and exposed groups were married and most of them reside at the Ibadan North Local Government area.

**Table 4.1: Socio Demographic Data of the Unexposed Group**

| Variable | Variables n (%) |
|---|---|
| **Sex** | |
| Male | **58 (68.2)** |
| Female | 27 (31.8) |
| **Age Group** | |
| 19-25 | 18 (21.18) |
| 25-40 | **52(61.18)** |
| Above 40 | 15 (17.65) |
| **Marital Status** | |
| Married | **51 (60)** |
| Single | 32 (37.6) |
| Divorce | 2 (2.4) |
| **Local Government Area of Residence** | |
| Ibadan North | 49 (57.6) |
| Lagelu | 24 (28.2) |
| Oluyole | 2 (2.4) |
| Ibadan Northwest | 10 11.8) |

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Source: Author's Field Work, 2023.

**Table 4.2 Socio Demographic Data of the Exposed Group**

| Variable | Variables n (%) |
|---|---|
| **Sex** | |
| Male | 54 (67.5) |
| Female | 26 (32.5) |
| **Age Group** | |
| 19-25 | 19(23.8) |
| 25-40 | 38(47.5) |
| Above 40 | 23 (28.8) |
| **Marital Status** | |
| Married | 54 (67.5) |
| Single | 25 (31.3) |
| Divorce | 1 (1.2) |
| **Local Government Area of Residence** | |
| Ibadan North | 47 (58.8) |
| Lagelu | 25 (31.3) |
| Oluyole | 3 (3.8) |
| Ibadan Northwest | 5 (6.3) |

Source: Author's Field Wok, 2023

## 4.2 Anthropometric Data of the Study Participants

### 4.2.1 Weight, Height, and Blood Pressure of the Unexposed group.

The Mean ± Standard deviation of the weight of unexposed groups is 67.89 ± 8.38, while the Mean ± Standard deviation 169.26 ± 6.82 of the height of unexposed group. Meanwhile, the Mean ± Standard deviation of the blood pressure (BP) is as follows; systolic BP is 122.15 ± 4.29, diastolic BP 79.55± 8.39 as presented in Table 4.3.

### 4.2.2 Weight, Height, and Blood Pressure of the Exposed group.

The Mean ± Standard deviation of the weight of exposed groups is 70.05 ± 7.46, while the Mean ± Standard deviation 170.59 ± 7.72 of the height of exposed group. Meanwhile, the Mean ± Standard deviation of the blood pressure (BP) is as follows; systolic BP is 121.09 ± 4.08, diastolic BP 79.49± 8.13 as presented in Table 4.4

**Table 4.3: Weight, Height, and Blood Pressure Distribution of the Unexposed Group**

| Variables | Mean ± SD |
|---|---|
| **Weight (kg)** | 67.89 ± 8.38 |
| **Height (cm)** | 169.26 ± 6.82 |
| **Blood Pressure** | |
| Systolic | 122.15 ± 4.29 |
| Diastolic | 79.55± 8.39 |

Source: Author's Field Work. 2023

**Table 4.4: Weight, Height, and Blood Pressure of the Exposed Group**

| Variables | Mean ± SD |
|---|---|
| **Weight (kg)** | 70.05 ± 7.46 |
| **Height (cm)** | 170.59 ± 7.72 |
| **Blood Pressure** | |
| Systolic | 121.09 ± 4.08 |
| Diastolic | 79.49± 8.13 |

Source: Author's Field Work. 2023.

### 4.2.3 Mean Comparison of the Anthropometric Data of the Unexposed and the Exposed

Table 4.5 shows the mean comparison of the anthropometric data of the unexposed and the exposed group using independent sample T-test. As shown in the table 4.5, there is no significant differences (P>0.05) between the mean weight, height, systolic pressure and diastolic pressure of the unexposed group and the exposed group respectively. This is very important in research like this. A difference in their anthropometric data could introduce bias in the subsequent clinical data that might emerge from the study,

### 4.2.4 Distribution of the Body Mass Index (BMI) in the Unexposed Group

Table 4.6 shows the distribution of the body mass index (BMI) among the participants in the unexposed groups. Their BMI is divided into underweight, healthy weight, overweight and obese. Among the eighty (85) participants recruited as the unexposed, three (3) people had underweight BM (<18.5) with the percentage 3.5%. Most of the participants; fifty-three (53) in number 62.4% had a healthy BMI (18.5 - 24.9). Twenty-eight (28) 32.9% of the participants were overweight with the BMI range of 25-29.9. While one (1) 1.2 % of the unexposed participants was obese with a BMI greater than 30.

### 4.2.5 Distribution of the Body Mass Index (BMI) in the Exposed Group

Table 4.7 shows the distribution of the body mass index (BMI) among the participants in the exposed groups. Their BMI is divided into underweight, healthy weight, overweight and obese. Among the eighty (80) participants recruited as the exposed, from the table 4.7 there was no participant who had underweight BM (<18.5). Just like the unexposed group, most of the participants; fifty (50) in number 65.2% had a healthy BMI (18.5 - 24.9). Twenty-eight (28) 35.0% of the participants were overweight with the BMI range of 25-29.9. While two (2) 2.5 % of the case participants were obese with a BMI greater than 30.

**Table 4.5: Mean Comparison of the Anthropometric Data**

| Anthropometric Data | Unexposed | Exposed | p- value |
|---|---|---|---|
| Weight (kg) | 67.89 ± 8.38 | 70.05 ± 7.46 | 0.083 |
| Height (cm) | 169.26 ± 6.82 | 170.59 ± 7.72 | 0.242 |
| Systolic B.P. | 122.15 ± 4.29 | 121.09 ± 4.08 | 0.105 |
| Diastolic B.P. | 79.55± 8.39 | 79.49± 8.13 | 0.952 |

Source: Author's Field Work. 2023.

**Table 4.6: The Distribution of the Body Mass Index (BMI) in Unexposed.**

| Category | BMI | Frequency | Percentage (%) |
|---|---|---|---|
| Underweight | <18.5 | 3 | 3.5 |
| Healthy weight | 18.5-24.9 | 53 | 62.4 |
| Overweight | 25-29.9 | 28 | 32.9 |
| Obese | >30.0 | 1 | 1.2 |
| | Total | 85 | 100.0 |

Source: Author's Field Work. 2023

**Table 4.7: The Distribution of the Body Mass Index (BMI) in Exposed**

| Category | BMI | Frequency | Percentage (%) |
|---|---|---|---|
| Underweight | <18.5 | 0 | 0 |
| Healthy weight | 18.5-24.9 | 50 | 62.5 |
| Overweight | 25-29.9 | 28 | 35 |
| Obese | >30.0 | 2 | 2.5 |
| | Total | 80 | 100.0 |

Source: Author's Field Work. 2023

### 4.3 Clinical Laboratory Data of the Study Participants

**4.3.2 SARS-CoV-2 Antibody Assay.** 80 participants who tested positive to SARS-CoV-2 RT-PCR method also tested positive to SARS-CoV-2 antibody. While 85 participants who tested negative to SARS-CoV-2 RT-PCR method also tested negative to SARS-CoV-2 antibody.

**4.3.3 Glycosylated Haemogloin (HBA1C) Assay.** The Mean ± Standard deviation haemoglobin value for the unexposed samples is 5.25 ± 0.39 while the haemoglobin value for the exposed is 5.18 ± 0.42. As presented in table 4.8 there is no significant differences ($p > 0.05$) between the mean of the unexposed group and the exposed group respectively.

**4.3.4 Predictive Renal Marker (Cystatin C) Analysis.** In figure 4.2 the cystatin C result (Mean ± SD) of the unexposed (0.76 ± 0.25) is higher than that of the exposed. However, looking at the Table 4.9, there is no significant difference ($p > 0.05$) between the mean of the unexposed group and the exposed group.

**Table 4.8: Mean comparison of HBA1C in Unexposed and Exposed**

| Analyte | Unexposed | Exposed | p- value |
|---|---|---|---|
| HBA1C | 5.25 ± 0.39 | 5.18 ± 0.42 | 0.259 |

Source: Author's Field Work. 2023

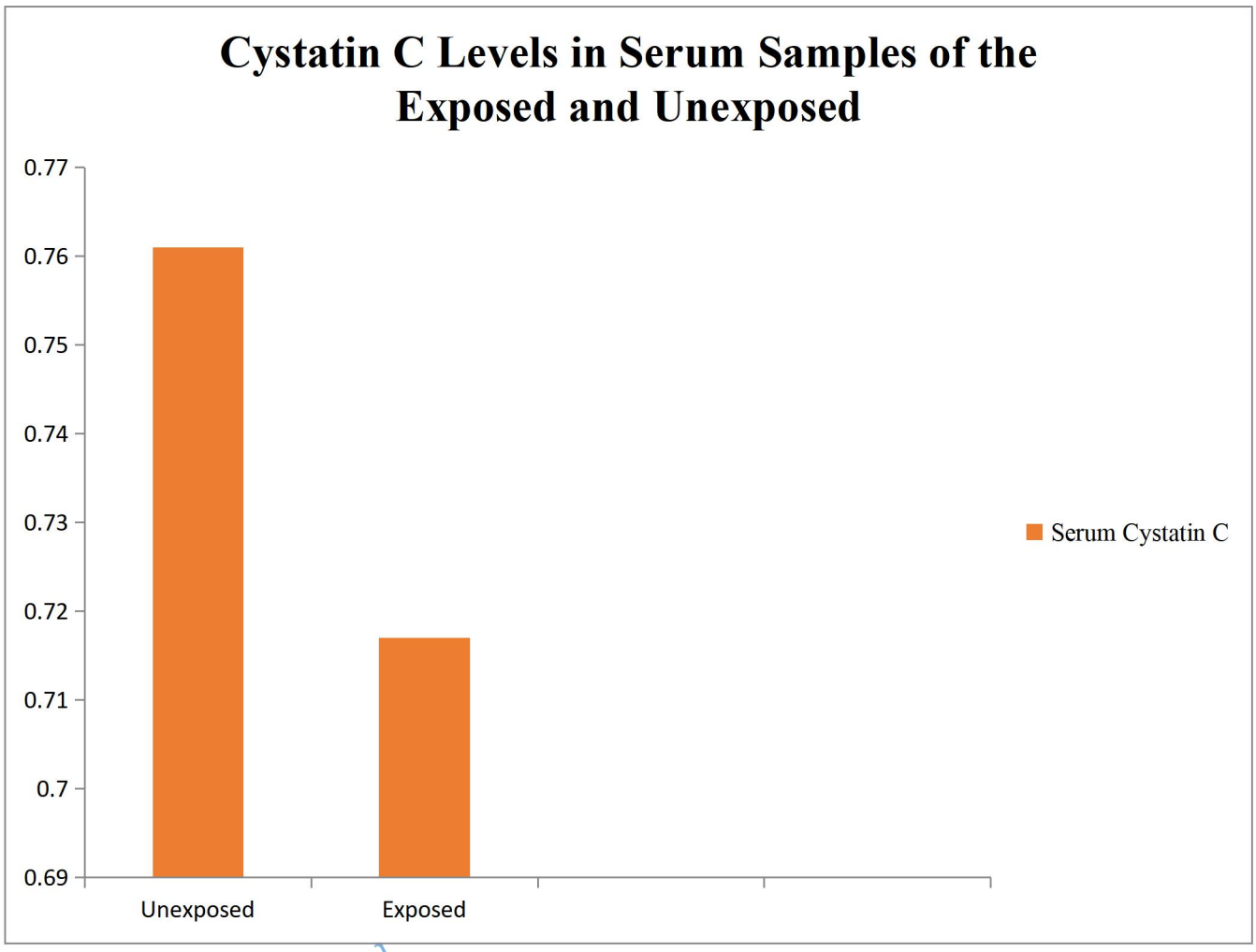


**Figure 4.2: Predictive Renal Marker (Cystatin C) of the Unexposed and Exposed Group.**

Source: Author's Field Work, 2023

**Table 4.9: Predictive Renal Marker (Cystatin C)**

| Analyte | Unexposed | Exposed | p- value |
|---|---|---|---|
| Cystatin C (mg/dl) | 0.76 ± 0.25 | 0.72 ± 0.18 | 0.202 |

Source: Author's Field Work, 2023

### 4.3.5 Renal Markers (Electrolytes, Urea, and Creatinine).

Table 4.9.1 shows the relationship between the mean values of electrolytes of unexposed and exposed, it also shows that there is no significant difference ($p > 0.05$) between the mean values of the electrolytes, urea, and creatinine of the unexposed and exposed group.

**Table 4.9.1: Renal Markers (Electrolytes, Urea and Creatinine)**

| Renal Markers | Unexposed | Exposed | p-value |
|---|---|---|---|
| $Na^+$ (mmol/L | 139.24 ± 2.728 | 139.68 2.782 | 0.307 |
| $K^+$ mmol/L | 3.945 ± 0.3386 | 3.971 ± 0.2926 | 0.592 |
| $CL^-$ mmol/L | 101.34 ± 3.045 | 102.02 ± 2.311 | 0.108 |
| $HCO_3^-$ mmol/L | 23.53 ± 2.950 | 23.02 ± 1.903 | 0.197 |
| Urea (mg/dl) | 20.94 ± 5.838 | 22.59 ± 5.158 | 0.057 |
| Cr (mg/dl) | 0.821 ± 0.1878 | 0.829 ± 0.2124 | 0.808 |

Source: Author's Field Work, 2023.

**4.3.6. Markers of inflammation and Thyroid Function** Table 4.9.2 shows the relationship between the inflammatory marker and the thyroid function markers of the exposed and the unexposed groups. There is no significant difference ($p > 0.05$) between the mean value of the inflammatory marker (C-reactive protein) of the unexposed group and that of exposed group. There are also no significant differences ($P>0.05$) between the mean values of thyroid function markers (Free Tri-iodothyronine (FT3), Free Thyroxine (FT4) and Thyroid stimulating hormone (TSH) of the unexposed group and the exposed group.

4.3.7. **Prevalence of Renal Dysfunction in Exposed.** Table 4.9.3 shows the prevalence of renal dysfunction in SARS-COV-2 exposed individuals. All the renal parameters analyzed had their ranges within the normal reference limit, while 1.3 % of the population of the cases had their serum sodium level above the normal reference range.

4.3.8 **Prevalence of inflammation and thyroid dysfunction in Exposed.** Table 4.9.4 shows the prevalence of inflammation and thyroid dysfunction in SARS-COV-2 exposed individuals. In table 4.9.4, all the participants had their inflammatory markers and thyroid markers within the normal reference ranges.

**Table 4.9.2: Markers of Inflammation and Thyroid Function**

| Biomarkers | Unexposed | Exposed | p-value |
|---|---|---|---|
| **Marker of inflammation** | | | |
| C-reactive protein (CRP) mg/L | 1.21 ± 1.0 | 1.37 ± 1.12 | 0.347 |
| **Thyroid function Markers** | | | |
| Free Tri-iodothyronine (FT3) pmol/L | 3.89 ± 0.439 | 3.86 ± 0.454 | 0.838 |
| Free Thyroxine (FT4) pmol/L | 15.2 ± 2.67 | 15.89 ± 2.48 | 0.098 |
| Thyroid Stimulating Hormone (TSH) mIU/L | 1.62 ± 1.04 | 1.41 ±0 .975 | 0.194 |

Source: Author's Field Work, 2023.

**Table 4.9.3: Prevalence of Renal Dysfunction in Exposed**

| Biomarker | Exposed (n=80) Mean ± SD | Reference Range | Low | Normal | Elevated | % with elevated level |
|---|---|---|---|---|---|---|
| $Na^+$ (mmol/L | 139.68 2.78 | 135 - 145 | 3 | 76 | 1 | 1.3 |
| $K^+$ mmol/L | 3.97 ± 0.29 | 3.5 -5.0 | 0 | 80 | 0 | 0 |
| $CL^-$ mmol/L | 102.02 ± 2.3 | 95 - 110 | 0 | 80 | 0 | 0 |
| $HCO_3^-$ mmol/L | 23.02 ± 1.90 | 20 - 30 | 2 | 0 | 0 | 0 |
| Urea (mg/dl) | 22.59 5.158 | 15 - 45 | 24 | 56 | 0 | 0 |
| Cr (mg/dl) | 0.829 ± 0.21 | 0.5 - 1.5 | 2 | 78 | 0 | 0 |
| Cys C (mg/L) | 0.72± 0.181 | 0.6-1.5 | 17 | 63 | 0 | 0 |

Source: Author's Field Work, 2023.

**Table 4.9.4: Prevalence of Inflammation and Thyroid Dysfunction in Exposed**

| Biomarker | Exposed (n=80) Mean ± SD | Reference Range | Low | Normal | Elevated | % with elevated level |
|---|---|---|---|---|---|---|
| **Marker of inflammation** | | | | | | |
| (CRP) mg/L | 0.717 ± 0.181 | 0.6-1.5 | 17 | 63 | 0 | 0 |
| **Thyroid function Markers** | | | | | | |
| FT3 pmol/L | 3.86 ± 0.454 | 3.4-5.2 | 0 | 80 | 0 | 0 |
| FT4 pmol/L | 15.89 ± 2.48 | 10.6-23.0 | 0 | 80 | 0 | 0 |
| TSH mIU/L | 1.41 ±0 .975 | 0.3-4.5 | 0 | 80 | 0 | 0 |

Source: Author's Field Work, 2023.

### 4.4. Discussion

From the total number (270) of the participants as presented in the results, 80 people tested positive for SARS-CoV-2 antibody. This shows 29.63% sero-prevalence in the study population. This is a variation to a study that was conducted among the health workers in the University College Hospital Ibadan, which shows a sero-prevalence 45.1%[1]. This could be because health workers being at the frontline of the pandemic are more exposed than others in society. During the pandemic the medical/health workers were particularly prone to being infected because of direct involvement in sample collection, surveillance, treatment, and follow-up.

However, research conducted before the introduction of the SARS- CoV-2 vaccine between December 2020 and March 2021 in the six geopolitical zones in Nigeria, showed a sero-prevalence of 66.8% in Nigeria which shows fairly good herd immunity during the peak of the pandemic[2]. Another cross-sectional study involving 4,904 participants reported a higher seroprevalence of 78.9% across 12 states in Nigeria. It was observed that seropositivity was consistent across the states surveyed from 69.8% in Lagos to 87.7% in Borno. This showed higher sero-prevalence after the introduction of vaccine. The result from the study also suggested that COVID-19 infection was prevalent in Nigeria despite the low hospitalization rate recorded as at the time of sampling[3].

Furthermore, the low sero-prevalence rate observed in this study is not unexpected which could be due to the fact that unexposed individuals who tested negative to SARS-CoV-2 infection through RT-PCR method were intentionally recruited for the survey as unexposed, due to the intended nature of the survey. Moreso, naturally acquired SARS-CoV-2 immunity persists for up to 11 months after infection, after which it wanes[4].

The Mean ± SD of the predictive renal markers between the unexposed and the exposed did not show any significant difference ($p > 0.05$). When compared statistically. This suggests that individuals who tested positive for SARS-CoV-2 infection during the pandemic fully recovered from any renal impairment that may have occurred during the infection. Another possibility is that a lower prevalence of renal impairment may have occurred in Ibadan during the active phase of the infection. However, during the active phase of infection with SARS-CoV-2 there were studies outside Nigeria that reported a high concentration of serum cystatin C in many patients which were associated with higher COVID-19 severity and mortality[5, 6, 7]. Meanwhile elevated levels of Cystatin C in individuals with COVID-19 are likely to indicate the existence of renal impairment such as acute kidney injury, they may also be a sign pf the excessive systemic inflammation and pro-oxidant state that distinguishes patients with COVID-19[6].

The result from this research is focused on the post pandemic effect of SARS-CoV-2 infection on renal function and the results suggest that individuals who were once exposed do not have post exposure renal dysfunction. However, this is in variant to research that suggested growing evidence of decline in renal function in the 6–12-month follow-up period in patients without any signs of AKI during the acute phase[8].

**4.6: Discussion on Markers of Renal Dysfunction (Electrolytes).**

The Mean ± SD of the electrolyte (Sodium, Potassium, Chloride and Bicarbonate) between the unexposed and the exposed did not show any significant difference ($p>0.05$). This suggests there are no electrolyte imbalances after been initially exposed to COVID-19. Meanwhile electrolyte imbalances were reported during active infection as highly prevalent in COVID-19 patients. Research showed that Hyponatremia, hypernatremia, and hypercalcemia were associated with poor COVID-19 outcome and the association is independent of the levels of inflammatory

markers[9]. Another research showed electrolyte imbalance in COVID-19 patients admitted to the emergency departmemt[10].

As suggested in the study, there are no electrolyte imbalances in individuals after being initially infected with COVID-19. However, a case was reported of persistent hypokalemia in a patient after more than five months since he was diagnosed with COVID-19. He was also reported to have prolonged hypomagnesemia and if not followed up closely, this could lead to life threatening arrythmias and seizure[11].

The Mean ± SD of urea and creatinine between the unexposed and the exposed did not show any significant difference ($p>0.05$). This suggests that there is no kidney dysfunction after been initially exposed to COVID-19. Meanwhile kidney dysfunctions were commonly reported during active infection with SARS-CoV-2[12, 13, 14]. This could be because the kidney is one of the extra pulmonary organs that express receptor (ACE-2) for SARS-CoV-2. And it could also be due to the hyponatremia commonly experienced due the SARS-CoV-2. Infection, with impact on the kidney function[14, 15].

Meanwhile, this study suggests there is no post exposure kidney dysfunction in Ibadan which is different from a multinational cohort study (involving the United States of America, Singapore, France, Spain, and Italy) that observed COVID-19 associated acute kidney injury been associated with worse long-term post AKI kidney function recovery[16].

However, a single center retrospective study conducted in Turkey and published in Nigeria Journal of clinical practice, observed that those who survived the mild/moderate and severe clinical manifestation of COVID-19 did not exhibit any risk of kidney outcomes after the acute phase of the disease, and the study could imply that the kidney can protect itself over a long period of time[17]. This research agrees with what was observed in Ibadan, Nigeria as documented above.

The inflammatory markers for the exposed group (Mean ± SD) is higher than that of the unexposed, however it is not statistically significant ($p>0.05$).

Cytokine storm is usually observed in exposed individuals due to overwhelming response of the immune system to the virus. This cytokine storm can cause several severe clinical complications[18].

However, results obtained from this study show a good recovery from inflammation after the pandemic. This is different from what was observed in a study done in Egypt that observed a significantly higher ($p < 0.005$) CRP in COVID-19 survivor and they concluded that exposed individuals have residual significant clinical and biochemical alterations that necessitate comprehensive medical care and close follow-up for longer period[19].

From this study, there is no significant difference ($p>0.05$) in the (Mean ± SD) of FT3, FT4 and TSH of the unexposed group compared to the exposed group. This suggests there are no post thyroid dysfunction in exposed individuals in Ibadan, Nigeria. However, during the active phase of infection, it was reported that the thyroid gland and SARS-CoV-2 infection interact intricately through hormones and immunomodulatory signaling molecules[20]. Therefore, thyroid dysfunctions (like thyroiditis, thyrotoxicosis, nonthyroidal illness syndrome, hypothyroidism and hyperthyroidism) were observed. This is not surprising because thyroid gland is also one of the extra pulmonary organs that express receptor (ACE-2) for SARS-CoV-2[20].

During the pandemic, many investigations noted cases of primary hypothyroidism linked to COVID-19. In a particular study, 5.2% (15/287) of patients experienced primary hypothyroidism, which was subclinical in 90% of instances (FT3 and FT4 were within reference limits), but higher than upper limit of the reference range in the remaining 10% [21] . Also, the authors

discovered that the in-hospital death rate for COVID-19 patients with hypothyroidism was higher than it was for COVID-19 patients with euthyroidism [21] . Hypothyroidism therefore may have negative consequences on the results of COVID-19, similar to thyrotoxicosis but perhaps to a lower level. A report of individuals with COVID-19 admitted to high intensity care units had two additional episodes of primary hypothyroidism caused by chronic autoimmune thyroiditis (CAT) [22] . It appears that primary hypothyroidism manifested in both of these instances during COVID-19 and persisted after discharge. Seven days following mild COVID-19 resolution, a case report of overt primary hypothyroidism caused by CAT was reported. There is some evidence to suggest that primary hypothyroidism may develop during or after COVID-19[23]

However, results from this research suggests there are no post thyroid dysfunction in exposed individuals in Ibadan which is different from reports stated above and other reports showing manifestation of thyroid disease (Hashimoto thyroiditis, Graves's disease and subacute thyroiditis) after COVID-19 infection[24].

A study also carried in India showed that out of 670 patients exposed 16 of them presented with post Covid-19 sub-acute thyroiditis[25].

## Endnote


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# Chapter Five

# Conclusion

## 5.1 Summary of Findings

There is a lot of growing interest in the effect of SARS-CoV-2 viral infection on both morbidity and mortality rate all over the world. This has led to several researches and inventions to quickly combat the pandemic. However, as the virus claimed lives all over the world and many also recovered from the infection, there is paucity of information regarding the post exposure effect of the virus on other vital organs apart from the lungs in Nigeria. This study focused on the post pandemic effect of SARS-CoV-2 viral infection on renal function, thyroid function and inflammatory markers. This study shows that there is no significant difference between the electrolytes (Sodium, Potassium, Chloride and Bicarbonate) of the non-exposed (control) and case (exposed). It also shows that there is no significant difference between the other renal markers (Urea and creatinine) of the control and the case. The predictive marker of kidney injury was also analyzed and there was no significant difference between the predictive marker (Cystatin-C) of kidney injury between the control and the case groups.

The marker of inflammation (C-reactive protein) analyzed and compared between the two groups also did not reflect any significant difference between the groups.

Thyroid function test (FT3, FT4, TSH) was also carried out in the two groups and there was no significant difference between they thyroid functions of the control group and the case group.

## 5.2: Conclusion

Many countries are still battling the post pandemic effect of the virus and many researches are ongoing to see the effect of the virus on health care system, it's worthy of note to imply from this study that the effect of the virus on renal, thyroid functions and inflammatory markers are statistically insignificant in Ibadan, South western part of Nigeria.

## 5.3: Recommendations

Based on the outcome of this study, the following are therefore recommended.

1. The clinicians and health care workers should be sensitized about the fact that SARS-CoV-2 viral infection has no post pandemic effects on the renal function, thyroid function and markers of inflammation.
2. The public should be sensitized that anyone who was exposed during the pandemic and had AKI during the active phase but eventually recovered, does not necessarily need to consistently visit clinics for a checkup, but should maintain a healthy lifestyle.

## 5.4: Contribution to Knowledge

In Nigeria, and particularly Ibadan, there is a paucity of information on the post-pandemic effect of SARS-CoV-2 viral infection on renal function, thyroid function, and inflammatory markers. This study was aimed at providing information. The study elucidated the effect of SARS-CoV-2 viral infection on renal function, thyroid function, and inflammatory marker. And the study

implies that post exposure to SARS-CoV-2 viral infection does not have any adverse effect on the renal function, thyroid function and inflammatory markers in individuals exposed in Ibadan, Nigeria.

This means that there is no need for panic and unnecessary frequent visits to health care centers because of been previously exposed to SARS-CoV-2 viral infection.

**5.5: Suggestion for Further Studies.**

Further studies should be carried out to determine the post-pandemic effect of SARS-CoV-2 viral infection on other vital organs that express SARS-CoV-2 receptor. This would provide good information to the clinician in handling the post- pandemic effect of SARS-CoV-2 viral infection on studied organs in exposed individuals and thereby reducing morbidity/mortality rate arising from the infection.

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## Appendix I

## Consent Form

Assessment of the Post-pandemic Renal and Thyroid Health of SARS-CoV-2 Exposed Individuals in Ibadan, Nigeria

Dear Respondent,

Ogunleye Temitope David, a Postgraduate Student of the Department of Biological Sciences, Faculty of Natural and Applied Sciences, Lead City University, Ibadan.

a. Is Conducting a Study on the Assessment of the Post-Pandemic Renal and Thyroid Health of SARS-CoV-2 Exposed Individuals in Ibadan
b. I would appreciate your participation in this Study which will involve us asking you a few questions regarding your experience with exposure to SARS-Cov-2 Virus, and your general wellbeing.
c. The Survey will take about 5 Minutes to complete and whatever information you provide will be kept strictly confidential. The study will not pose any threat to you, and you Are free to withdraw from participating at any time.

Thank you for your time.

If you agree to participate in this study please tick this Box [ ]

**Appendix II**

**Questionnaire.**

The information provided will be kept confidential and please do not write your name on it.

Kindly spare a few minutes of your valuable time to answer the questions.

**SECTION A: SOCIO-DEMOGRAPHIC CHARACTERISTICS OF RESPONDENTS**

1. Age as at Last Birthday; …… Years

2. Sex: Male [ ] Female [ ]

3. Marital Status: A. Single [ ] B. Married [ ] C. Divorced [ ] D. Widowed [ ] E. Separated [ ] F. Others (Please Specify).

4. Occupation:

5. Educational Attainment: A. No Formal Education [ ] B. Primary Education [ ] C. Secondary Education [ ] D. Tertiary Education [ ]

6. Place of residence_____

**SECTION B: ANTHROPOMETRIC MEASUREMENT**

1. Weight_____
2. Height_____
3. Body mass Index (BMI)_____
4. Blood Pressure_____

**SECTION C: LIFESTYLE (HISTORY)**

1. Cigarette smoking? Before (1) Presently (2) Never (3)
2. If presently, how? Daily (1) Weekly (2) Occasionally (3)
3. Alcohol intake? Daily (1) Weekly (2) Occasionally (3) Never (4)
4. Vegetables and fruit intake? Daily (1) weekly (2) occasionally (3

**SECTION D: MEDICAL HISTORY**

1. Do you have any medical condition being managed?

If Yes, Kindly state it_____, and when did it start_____?

2. What medication are you presently on? _____

Have you had any of the following symptoms in the past eight months?

- Cough a) Yes____ b) No_____
- Sore Throat a) Yes____ b) No_____
- Fever a) Yes____ b) No_____
- Fatigue/Tiredness a) Yes____ b) No_____
- Loss of taste or smell a) Yes____ b) No_____
- Diarrhea a) Yes____ b) No_____
- Aches and Pains a) Yes____ b) No_____
- Rash on skin or discoloration of fingers or toes a) Yes____ b) No_____
- Difficulty breathing or shortness of breath a) Yes____ b) No_____
- Chest Pain a) Yes____ b) No_____
- Loss of speech or mobility or confusion a) Yes____ b) No_____
- Have you ever been diagnosed with acute kidney disease/injury? a) Yes____ b) No_____

**SECTION E TEST HISTORY.**

- Did you ever test for COVID-19 in the past eight months? a) Yes____ b) No___
- Where were you tested? _____
- Do you have an idea of the method of assay? a) Rapid Testing_____ b) PCR _____
- What was the result a) Positive____ b) Negative_____ c) Indeterminate?

**SECTION F: VACCINATION HISTORY**.

- Have you received the COVID-19 Vaccine? a) Yes____ b) No_____
- If yes, when were you vaccinated? _____
- Are you fully vaccinated _____
- Did you receive any booster dose of the vaccine after fully vaccinated_____
- What type of Covid Vaccine did you receive_____

Did you feel any of the symptoms below after vaccination?

- Cough a) Yes____ b) No_____
- Sore Throat a) Yes____ b) No_____
- Fever a) Yes____ b) No_____
- Fatigue/Tiredness a) Yes____ b) No_____
- Loss of taste or smell a) Yes____ b) No_____
- Diarrhea a) Yes____ b) No_____
- Aches and Pains a) Yes____ b) No_____
- Rash on skin or discoloration of fingers or toes a) Yes____ b) No_____
- Difficulty breathing or shortness of breath a) Yes____ b) No_____

- Chest Pain a) Yes____ b) No_____
- Loss of speech or mobility or confusion a) Yes____ b) No_____

Source: Author's Field Work, 2023.

**Appendix III**

**Raw Data from Laboratory Analysis (Control)**

| S/N | CRP | CysC | FT3 | FT4 | TSH | Urea | Creat | Na | K | Cl | $HCO_3$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | 0.4 | 0.7 | 4.1 | 11.5 | 2.21 | 17.0 | 1.2 | 144.0 | 3.6 | 105.0 | 25.0 |
| 2. | 0.9 | 0.5 | 3.64 | 15.8 | 3.32 | 28.0 | 1.1 | 141.0 | 4.1 | 106.0 | 21.0 |
| 3. | 0.3 | 0.7 | 4.59 | 17.9 | 0.993 | 42.0 | 0.7 | 140.0 | 3.8 | 100.0 | 22.0 |
| 4. | 0.6 | 0.8 | 5.22 | 12.1 | 3.51 | 23.0 | 0.8 | 139.0 | 4.4 | 100.0 | 25.0 |
| 5. | 2.0 | 1.0 | 4.36 | 12.9 | 2.222 | 21.0 | 0.9 | 136.0 | 4.1 | 98.0 | 24.0 |
| 6. | 3.3 | 0.9 | 4.52 | 14.3 | 0.876 | 19.0 | 0.9 | 138.0 | 4.0 | 101.0 | 23.0 |
| 7. | 4.1 | 1.0 | 4.58 | 17.9 | 0.543 | 40.0 | 0.5 | 140.0 | 4.2 | 102.0 | 24.0 |
| 8. | 1.1 | 0.8 | 3.78 | 20.0 | 1.123 | 25.0 | 0.5 | 144.0 | 3.6 | 105.0 | 25.0 |
| 9. | 1.1 | 0.9 | 3.99 | 19.3 | 1.78 | 17.0 | 0.8 | 139.0 | 4.9 | 104.0 | 22.0 |
| 10. | 0.2 | 0.8 | 4.25 | 16.4 | 0.7 | 18.0 | 0.7 | 137.0 | 4.3 | 96.0 | 27.0 |
| 11. | 0.2 | 0.7 | 3.7 | 13.8 | 0.9 | 26.0 | 1.0 | 136.0 | 3.8 | 96.0 | 26.0 |
| 12. | 0.2 | 0.7 | 4.6 | 12.5 | 0.8 | 14.0 | 0.9 | 137.0 | 4.2 | 96.0 | 27.0 |
| 13. | 0.2 | 0.5 | 3.8 | 16.9 | 1.41 | 29.0 | 1.0 | 141.0 | 3.6 | 102.0 | 25.0 |
| 14. | 0.5 | 1.1 | 3.3 | 12.7 | 1.8 | 26.0 | 1.0 | 137.0 | 4.0 | 102.0 | 21.0 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 15. | 1.5 | 0.5 | 3.42 | 15.3 | 1.4 | 17.0 | 0.6 | 142.0 | 4.1 | 102.0 | 36.0 |
| 16. | 0.4 | 0.8 | 4.61 | 12.7 | 0.895 | 23.0 | 0.9 | 139.0 | 3.8 | 104.0 | 21.0 |
| 17. | 0.2 | 0.8 | 3.51 | 13.6 | 2.21 | 22.0 | 1.0 | 141.0 | 3.9 | 107.0 | 20.0 |
| 18. | 0.5 | 0.7 | 3.5 | 16.2 | 1.89 | 12.0 | 0.9 | 137.0 | 4.0 | 99.0 | 21.0 |
| 19. | 1.5 | 0.9 | 4.0 | 18.8 | 2.51 | 14.0 | 0.5 | 140.0 | 3.8 | 101.0 | 21.0 |
| 20. | 0.4 | 0.4 | 3.61 | 11.9 | 0.491 | 18.0 | 0.5 | 141.0 | 4.2 | 104.0 | 23.0 |
| 21. | 0.2 | 0.6 | 3.22 | 19.0 | 1.87 | 21.0 | 0.8 | 136.0 | 3.9 | 95.0 | 27.0 |
| 22. | 0.5 | 1.1 | 4.7 | 14.7 | 0.942 | 17.0 | 0.7 | 139.0 | 3.6 | 104.0 | 21.0 |
| 23. | 0.4 | 0.7 | 3.9 | 18.0 | 1.89 | 28.0 | 1.0 | 140.0 | 3.9 | 102.0 | 24.0 |
| 24. | 0.2 | 0.9 | 3.5 | 11.6 | 2.51 | 22.0 | 0.9 | 142.0 | 4.2 | 105.0 | 23.0 |
| 25. | 0.5 | 0.8 | 3.12 | 12.8 | 4.0 | 19.0 | 1.0 | 141.0 | 3.9 | 103.0 | 24.0 |
| 26. | 0.6 | 0.7 | 4.1 | 17.4 | 2.0 | 25.0 | 1.0 | 140.0 | 3.9 | 100.0 | 22.0 |
| 27. | 3.2 | 0.7 | 3.85 | 14.0 | 0.576 | 29.0 | 1.2 | 138.0 | 4.4 | 102.0 | 24.0 |
| 28. | 0.7 | 0.5 | 3.5 | 12.0 | 0.491 | 30.0 | 0.9 | 142.0 | 3.9 | 104.0 | 25.0 |
| 29. | 0.6 | 1.1 | 4.0 | 13.7 | 1.87 | 19.0 | 0.9 | 137.0 | 4.0 | 99.0 | 26.0 |
| 30. | 3.2 | 0.8 | 3.61 | 19.2 | 2.04 | 22.0 | 0.6 | 140.0 | 3.8 | 101.0 | 21.0 |
| 31. | 0.2 | 1.2 | 3.0 | 11.0 | 0.897 | 13.0 | 0.9 | 134.0 | 4.4 | 106.0 | 21.0 |
| 32. | 0.5 | 1.1 | 4.21 | 13.6 | 0.999 | 11.0 | 0.5 | 136.0 | 4.1 | 100.0 | 26.0 |
| 33. | 0.9 | 1.3 | 3.91 | 15.9 | 1.134 | 12.0 | 0.5 | 136.0 | 4.0 | 100.0 | 25.0 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 34. | 3.1 | 0.9 | 3.89 | 19.0 | 1.23 | 9.0 | 0.8 | 137.0 | 4.2 | 98.0 | 24.0 |
| 35. | 4.0 | 0.3 | 3.96 | 20.5 | 4.01 | 10.0 | 0.7 | 145.0 | 3.6 | 101.0 | 23.0 |
| 36. | 3.3 | 0.5 | 4.1 | 12.6 | 3.12 | 15.0 | 1.0 | 146.0 | 4.9 | 102.0 | 24.0 |
| 37. | 0.8 | 1.1 | 3.0 | 17.6 | 0.922 | 18.0 | 0.9 | 142.0 | 4.3 | 105.0 | 25.0 |
| 38. | 0.9 | 0.9 | 3.98 | 13.6 | 0.897 | 22.0 | 1.0 | 141.0 | 3.8 | 104.0 | 22.0 |
| 39. | 0.6 | 0.3 | 3.76 | 14.6 | 1.22 | 22.0 | 1.0 | 140.0 | 4.2 | 96.0 | 27.0 |
| 40. | 0.5 | 0.5 | 4.0 | 12.7 | 0.987 | 35.0 | 0.6 | 138.0 | 3.6 | 96.0 | 26.0 |
| 41. | 0.5 | 0.6 | 4.32 | 16.7 | 0.879 | 23.0 | 0.9 | 142.0 | 4.0 | 96.0 | 27.0 |
| 42. | 0.9 | 0.5 | 3.42 | 11.9 | 0.876 | 25.0 | 1.0 | 137.0 | 4.1 | 102.0 | 25.0 |
| 43. | 1.1 | 0.7 | 4.61 | 12.0 | 1.23 | 22.0 | 0.9 | 140.0 | 3.8 | 102.0 | 21.0 |
| 44. | 1.3 | 0.6 | 3.51 | 13.6 | 2.13 | 18.0 | 0.5 | 134.0 | 3.9 | 102.0 | 22.0 |
| 45. | 1.4 | 0.5 | 3.5 | 12.9 | 3.129 | 17.0 | 0.5 | 136.0 | 4.0 | 104.0 | 21.0 |
| 46. | 0.4 | 0.6 | 4.0 | 14.7 | 3.31 | 16.0 | 0.8 | 136.0 | 3.8 | 107.0 | 20.0 |
| 47. | 1.8 | 0.8 | 3.61 | 19.4 | 0.997 | 18.0 | 0.7 | 137.0 | 4.2 | 99.0 | 20.0 |
| 48. | 2.1 | 0.6 | 3.22 | 16.9 | 0.675 | 25.0 | 1.0 | 145.0 | 3.9 | 101.0 | 21.0 |
| 49. | 2.2 | 0.5 | 4.7 | 15.0 | 0.564 | 25.0 | 0.9 | 146.0 | 3.6 | 100.0 | 22.0 |
| 50. | 3.1 | 0.7 | 3.9 | 18.0 | 1.123 | 19.0 | 0.9 | 138.0 | 3.9 | 99.0 | 23.0 |
| 51. | 0.9 | 0.6 | 3.5 | 14.9 | 0.922 | 23.0 | 0.8 | 134.0 | 4.2 | 96.0 | 27.0 |
| 52. | 1.3 | 0.7 | 3.12 | 17.6 | 2.13 | 24.0 | 0.5 | 141.0 | 3.9 | 96.0 | 26.0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 53. | 0.8 | 0.7 | 4.1 | 15.8 | 0.786 | 19.0 | 0.8 | 140.0 | 3.9 | 96.0 | 21.0 |
| 54. | 0.9 | 0.8 | 3.96 | 17.0 | 0.852 | 26.0 | 0.6 | 139.0 | 4.4 | 102.0 | 25.0 |
| 55. | 0.1 | 1.1 | 4.21 | 14.6 | 0.522 | 17.0 | 1.1 | 136.0 | 3.9 | 102.0 | 21.0 |
| 56. | 0.3 | 1.1 | 4.22 | 16.9 | 0.487 | 23.0 | 0.9 | 138.0 | 4.0 | 102.0 | 36.0 |
| 57. | 0.6 | 1.2 | 3.81 | 18.9 | 0.535 | 21.0 | 0.7 | 140.0 | 3.8 | 104.0 | 21.0 |
| 58. | 1.3 | 0.9 | 3.98 | 14.6 | 0.682 | 15.0 | 1.0 | 144.0 | 3.3 | 107.0 | 20.0 |
| 59. | 1.1 | 0.7 | 3.76 | 14.8 | 1.12 | 23.0 | 0.9 | 139.0 | 3.5 | 99.0 | 26.0 |
| 60. | 1.6 | 0.7 | 4.0 | 16.8 | 2.34 | 24.0 | 0.9 | 137.0 | 3.3 | 101.0 | 21.0 |
| 61. | 1.8 | 0.6 | 4.12 | 16.4 | 4.13 | 19.0 | 0.8 | 136.0 | 3.7 | 100.0 | 22.0 |
| 62. | 2.2 | 0.5 | 3.63 | 17.9 | 3.21 | 26.0 | 0.5 | 137.0 | 3.5 | 99.0 | 23.0 |
| 63. | 3.1 | 0.9 | 4.21 | 20.0 | 0.987 | 17.0 | 0.8 | 141.0 | 3.6 | 102.0 | 23.0 |
| 64. | 0.9 | 1.2 | 4.21 | 18.7 | 1.9 | 23.0 | 0.6 | 137.0 | 4.0 | 102.0 | 21.0 |
| 65. | 1.3 | 0.4 | 3.91 | 17.9 | 2.23 | 26.0 | 1.1 | 142.0 | 3.8 | 102.0 | 25.0 |
| 66. | 0.8 | 0.6 | 3.89 | 19.8 | 3.21 | 17.0 | 0.9 | 139.0 | 3.3 | 104.0 | 21.0 |
| 67. | 0.9 | 0.7 | 3.96 | 13.4 | 3.41 | 23.0 | 0.9 | 134.0 | 3.5 | 107.0 | 20.0 |
| 68. | 0.6 | 0.7 | 4.1 | 10.7 | 4.32 | 22.0 | 0.9 | 138.0 | 3.3 | 99.0 | 26.0 |
| 69. | 0.7 | 0.5 | 3.0 | 11.6 | 1.12 | 12.0 | 0.8 | 136.0 | 3.7 | 101.0 | 21.0 |
| 70. | 2.3 | 1.1 | 3.98 | 13.8 | 3.4 | 14.0 | 0.5 | 141.0 | 3.5 | 100.0 | 22.0 |
| 71. | 3.3 | 0.8 | 3.76 | 16.9 | 0.922 | 18.0 | 0.8 | 140.0 | 3.6 | 99.0 | 23.0 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 72. 2.1 | 1.2 | 4.0 | 14.2 | 2.13 | 21.0 | 0.6 | 143.0 | 4.2 | 102.0 | 21.0 |
| 73. 0.6 | 1.1 | 4.32 | 19.7 | 0.786 | 17.0 | 1.1 | 139.0 | 3.9 | 104.0 | 23.0 |
| 74. 0.5 | 1.3 | 3.42 | 13.3 | 0.852 | 28.0 | 0.9 | 138.0 | 3.9 | 100.0 | 24.0 |
| 75. 0.7 | 0.9 | 4.61 | 11.9 | 0.522 | 22.0 | 0.7 | 136.0 | 4.4 | 99.0 | 26.0 |
| 76. 0.8 | 0.3 | 3.51 | 11.0 | 0.487 | 21.0 | 1.0 | 139.0 | 3.9 | 98.0 | 29.0 |
| 77. 1.1 | 0.5 | 3.5 | 13.2 | 0.535 | 20.0 | 0.9 | 140.0 | 4.0 | 105.0 | 23.0 |
| 78. 1.2 | 1.1 | 4.0 | 12.7 | 0.682 | 17.0 | 0.9 | 141.0 | 3.8 | 101.0 | 21.0 |
| 79. 3.2 | 0.9 | 3.66 | 13.4 | 1.12 | 16.0 | 0.8 | 139.0 | 3.6 | 103.0 | 22.0 |
| 80. 0.4 | 0.3 | 3.53 | 15.9 | 2.34 | 17.0 | 0.5 | 141.0 | 4.0 | 100.0 | 25.0 |
| 81. 1.2 | 0.5 | 3.72 | 13.3 | 0.987 | 23.0 | 0.8 | 139.0 | 4.1 | 108.0 | 26.0 |
| 82. 0.5 | 0.6 | 3.38 | 17.9 | 0.762 | 26.0 | 0.6 | 140.0 | 4.5 | 101.0 | 24.0 |
| 83. 0.8 | 0.5 | 4.21 | 16.2 | 1.344 | 17.0 | 1.1 | 141.0 | 4.8 | 102.0 | 23.0 |
| 84. 1.9 | 0.8 | 3.54 | 12.9 | 1.24 | 23.0 | 0.9 | 139.0 | 4.7 | 105.0 | 22.0 |
| 85. 2.0 | 0.9 | 3.67 | 11.9 | 3.42 | 22.0 | 0.8 | 141.0 | 3.6 | 101.0 | 19.0 |

Source: Author's Field Work, 2023

**Raw Data from Laboratory Analysis (Case)**

| S/N | CRP | CysC | FT3 | FT4 | TSH | Urea | Creat | Na | K | Cl | $HCO_3$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 0.2 | 0.8 | 3.5 | 12.1 | 0.49 | 17.0 | 0.8 | 143.0 | 3.6 | 101.0 | 23.0 |
| 2 | 0.4 | 0.5 | 3.12 | 11.9 | 0.782 | 28.0 | 0.8 | 141.0 | 3.8 | 102.0 | 23.0 |
| 3 | 0.6 | 0.6 | 4.1 | 14.6 | 0.982 | 22.0 | 1.1 | 137.0 | 4.2 | 100.0 | 23.0 |
| 4 | 0.6 | 0.6 | 3.96 | 17.8 | 0.852 | 21.0 | 0.9 | 144.0 | 4.1 | 105.0 | 25.0 |
| 5 | 3.8 | 0.9 | 4.21 | 18.9 | 0.567 | 20.0 | 0.9 | 142.0 | 4.0 | 108.0 | 20.0 |
| 6 | 0.7 | 0.9 | 4.22 | 18.2 | 1.23 | 19.0 | 0.8 | 142.0 | 4.0 | 105.0 | 23.0 |
| 7 | 1.1 | 0.7 | 3.81 | 20.1 | 3.14 | 22.0 | 0.8 | 137.0 | 3.8 | 99.0 | 24.0 |
| 8 | 0.5 | 0.8 | 3.98 | 15.8 | 2.46 | 29.0 | 0.6 | 142.0 | 4.5 | 106.0 | 23.0 |
| 9 | 0.9 | 0.9 | 3.76 | 16.7 | 2.78 | 10.0 | 0.4 | 141.0 | 3.8 | 101.0 | 21.0 |
| 10 | 1.2 | 0.8 | 4.0 | 13.5 | 2.26 | 17.0 | 0.4 | 139.0 | 3.6 | 103.0 | 22.0 |
| 11 | 3.5 | 0.5 | 4.12 | 15.6 | 0.982 | 14.0 | 0.7 | 141.0 | 4.0 | 100.0 | 25.0 |
| 12 | 0.4 | 0.6 | 3.63 | 16.9 | 1.567 | 19.0 | 0.9 | 139.0 | 4.1 | 108.0 | 26.0 |
| 13 | 0.6 | 1.1 | 4.21 | 14.8 | 0.098 | 21.0 | 1.0 | 140.0 | 4.5 | 101.0 | 24.0 |
| 14 | 0.6 | 1.0 | 4.21 | 19.2 | 2.35 | 23.0 | 0.9 | 141.0 | 4.8 | 102.0 | 23.0 |
| 15 | 3.8 | 0.8 | 3.91 | 11.0 | 0.976 | 26.0 | 0.6 | 139.0 | 4.7 | 105.0 | 22.0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 0.7 | 0.7 | 3.89 | 13.6 | 0.0562 | 29.0 | 0.9 | 141.0 | 3.6 | 101.0 | 19.0 |
| 17 | 1.1 | 0.8 | 3.96 | 15.9 | 0.765 | 27.0 | 0.9 | 143.0 | 3.6 | 101.0 | 23.0 |
| 18 | 0.5 | 0.6 | 3.0 | 19.0 | 0.8692 | 30.0 | 1.1 | 141.0 | 3.8 | 102.0 | 23.0 |
| 19 | 0.4 | 0.5 | 3.35 | 15.0 | 1.1 | 31.0 | 1.2 | 137.0 | 4.2 | 100.0 | 23.0 |
| 20 | 0.3 | 0.5 | 3.64 | 15.34 | 2.345 | 24.0 | 0.7 | 144.0 | 4.1 | 105.0 | 25.0 |
| 21 | 1.1 | 0.6 | 4.22 | 14.7 | 0.567 | 28.0 | 0.7 | 139.0 | 3.9 | 100.0 | 22.0 |
| 22 | 2.1 | 0.9 | 3.89 | 19.5 | 0.52 | 19.0 | 0.6 | 138.0 | 4.2 | 105.0 | 22.0 |
| 23 | 0.8 | 1.1 | 3.56 | 14.6 | 0.456 | 22.0 | 1.1 | 141.0 | 3.7 | 102.0 | 22.0 |
| 24 | 0.9 | 1.1 | 3.42 | 17.5 | 0.952 | 24.0 | 0.9 | 140.0 | 3.8 | 102.0 | 21.0 |
| 25 | 0.6 | 0.6 | 3.0 | 15.7 | 1.123 | 18.0 | 0.6 | 138.0 | 3.6 | 105.0 | 19.0 |
| 26 | 0.6 | 0.6 | 3.56 | 18.9 | 0.862 | 10.0 | 0.8 | 137.0 | 4.2 | 108.0 | 25.0 |
| 27 | 3.4 | 0.9 | 4.56 | 15.2 | 1.234 | 19.0 | 0.5 | 142.0 | 4.1 | 105.0 | 23.0 |
| 28 | 2.2 | 0.9 | 5.0 | 11.3 | 0.942 | 14.0 | 1.3 | 140.0 | 3.9 | 99.0 | 21.0 |
| 29 | 1.0 | 0.7 | 3.45 | 11.1 | 0.652 | 17.0 | 1.1 | 137.0 | 3.8 | 106.0 | 22.0 |
| 30 | 0.9 | 0.8 | 4.21 | 16.9 | 0.0567 | 19.0 | 1.0 | 133.0 | 4.1 | 101.0 | 25.0 |
| 31 | 0.7 | 0.9 | 3.92 | 15.7 | 2.134 | 24.0 | 0.8 | 131.0 | 3.6 | 103.0 | 22.0 |
| 32 | 0.1 | 0.8 | 3.89 | 18.9 | 1.24 | 28.0 | 0.9 | 145.0 | 3.6 | 100.0 | 23.0 |
| 33 | 0.9 | 0.5 | 4.1 | 20.0 | 2.23 | 29.0 | 0.7 | 147.0 | 3.8 | 99.0 | 24.0 |
| 34 | 0.6 | 0.6 | 3.46 | 15.3 | 0.987 | 16.0 | 0.9 | 132.0 | 4.2 | 101.0 | 25.0 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 35 | 0.1 | 0.6 | 4.21 | 16.3 | 1.123 | 22.0 | 1.1 | 141.0 | 4.1 | 102.0 | 26.0 |
| 36 | 2.3 | 0.9 | 4.21 | 14.7 | 4.02 | 22.0 | 1.1 | 140.0 | 3.9 | 105.0 | 27.0 |
| 37 | 2.4 | 0.9 | 3.91 | 17.8 | 3.46 | 31.0 | 0.9 | 138.0 | 4.2 | 101.0 | 20.0 |
| 38 | 4.0 | 0.7 | 3.89 | 16.9 | 4.12 | 20.0 | 1.2 | 138.0 | 3.7 | 101.0 | 21.0 |
| 39 | 1.0 | 0.8 | 3.96 | 17.3 | 3.78 | 36.0 | 1.2 | 141.0 | 3.8 | 99.0 | 26.0 |
| 40 | 3.2 | 0.9 | 3.0 | 12.5 | 3.675 | 19.0 | 0.9 | 140.0 | 3.6 | 101.0 | 22.0 |
| 41 | 1.2 | 0.8 | 3.35 | 12.0 | 0.908 | 24.0 | 0.7 | 139.0 | 4.4 | 100.0 | 21.0 |
| 42 | 3.1 | 0.5 | 3.64 | 13.7 | 0.965 | 26.0 | 0.6 | 138.0 | 4.1 | 103.0 | 24.0 |
| 43 | 2.1 | 0.6 | 4.22 | 19.4 | 0.624 | 19.0 | 0.6 | 137.0 | 3.9 | 101.0 | 25.0 |
| 44 | 0.3 | 0.9 | 3.89 | 16.3 | 0.942 | 14.0 | 0.5 | 139.0 | 4.2 | 99.0 | 26.0 |
| 45 | 0.4 | 1.0 | 3.56 | 11.8 | 0.786 | 17.0 | 0.7 | 141.0 | 3.8 | 100.0 | 22.0 |
| 46 | 0.5 | 0.7 | 3.42 | 13.3 | 1.23 | 19.0 | 0.8 | 140.0 | 4.2 | 105.0 | 20.0 |
| 47 | 3.2 | 0.6 | 3.0 | 14.5 | 0.567 | 31.0 | 0.9 | 136.0 | 3.8 | 104.0 | 20.0 |
| 48 | 2.2 | 0.4 | 3.56 | 11.9 | 0.879 | 32.0 | 0.9 | 135.0 | 4.0 | 101.0 | 22.0 |
| 49 | 1.0 | 0.5 | 4.56 | 16.4 | 1.23 | 22.0 | 0.5 | 139.0 | 3.9 | 103.0 | 25.0 |
| 50 | 1.5 | 0.8 | 5.0 | 12.7 | 2.56 | 28.0 | 0.5 | 140.0 | 4.2 | 102.0 | 21.0 |
| 51 | 2.6 | 0.9 | 3.45 | 17.3 | 4.1 | 25.0 | 0.8 | 138.0 | 4.5 | 101.0 | 22.0 |
| 52 | 3.1 | 0.5 | 4.21 | 15.2 | 0.98 | 29.0 | 0.7 | 138.0 | 4.4 | 100.0 | 25.0 |
| 53 | 0.1 | 0.6 | 3.92 | 14.6 | 0.522 | 23.0 | 1.0 | 137.0 | 3.9 | 104.0 | 23.0 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 54 | 0.6 | 0.9 | 4.57 | 17.1 | 0.678 | 26.0 | 0.9 | 141.0 | 4.0 | 102.0 | 25.0 |
| 55 | 0.8 | 0.9 | 4.21 | 14.5 | 0.456 | 19.0 | 1.0 | 140.0 | 3.8 | 102.0 | 23.0 |
| 56 | 0.2 | 0.7 | 3.98 | 11.9 | 1.13 | 30.0 | 1.0 | 142.0 | 3.6 | 102.0 | 24.0 |
| 57 | 4.0 | 0.8 | 5.11 | 18.5 | 1.457 | 18.0 | 0.6 | 143.0 | 3.5 | 104.0 | 22.0 |
| 58 | 0.1 | 0.9 | 3.1 | 14.5 | 0.896 | 23.0 | 0.9 | 144.0 | 3.8 | 101.0 | 26.0 |
| 59 | 2.2 | 0.8 | 3.42 | 16.2 | 0.666 | 25.0 | 1.0 | 142.0 | 3.9 | 99.0 | 24.0 |
| 60 | 0.9 | 0.5 | 3.67 | 18.9 | 0.563 | 29.0 | 0.9 | 139.0 | 4.0 | 101.0 | 22.0 |
| 61 | 1.1 | 0.6 | 3.87 | 17.3 | 1.78 | 21.0 | 0.9 | 137.0 | 3.8 | 100.0 | 21.0 |
| 62 | 3.2 | 0.9 | 4.32 | 18.8 | 1.467 | 24.0 | 0.7 | 136.0 | 4.2 | 99.0 | 22.0 |
| 63 | 3.0 | 1.0 | 4.89 | 17.3 | 1.7831 | 27.0 | 0.6 | 139.0 | 3.9 | 102.0 | 20.0 |
| 64 | 1.3 | 0.7 | 3.87 | 15.2 | 1.67 | 25.0 | 0.6 | 141.0 | 3.6 | 102.0 | 22.0 |
| 65 | 1.4 | 0.6 | 3.56 | 14.6 | 1.225 | 19.0 | 1.1 | 140.0 | 3.9 | 102.0 | 23.0 |
| 66 | 3.4 | 0.4 | 4.21 | 17.1 | 1.567 | 23.0 | 1.2 | 142.0 | 4.2 | 104.0 | 24.0 |
| 67 | 0.9 | 0.5 | 3.89 | 14.5 | 1.62 | 24.0 | 0.9 | 140.0 | 3.9 | 100.0 | 25.0 |
| 68 | 0.5 | 0.8 | 3.56 | 11.9 | 2.13 | 19.0 | 0.5 | 142.0 | 3.9 | 103.0 | 26.0 |
| 69 | 0.6 | 0.9 | 3.41 | 18.5 | 3.16 | 26.0 | 0.7 | 143.0 | 3.7 | 106.0 | 22.0 |
| 70 | 3.2 | 0.6 | 4.21 | 14.5 | 0.786 | 17.0 | 0.8 | 144.0 | 3.9 | 102.0 | 21.0 |
| 71 | 1.0 | 0.5 | 4.0 | 13.2 | 1.58 | 23.0 | 0.5 | 142.0 | 3.5 | 99.0 | 24.0 |
| 72 | 2.2 | 0.7 | 3.89 | 18.9 | 2.34 | 21.0 | 0.9 | 139.0 | 4.2 | 101.0 | 25.0 |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 73 | 2.1 | 0.6 | 3.67 | 14.5 | 1.16 | 15.0 | 1.1 | 137.0 | 4.4 | 98.0 | 26.0 |
| 74 | 0.8 | 0.4 | 3.46 | 19.3 | 0.982 | 24.0 | 0.7 | 136.0 | 4.6 | 99.0 | 21.0 |
| 75 | 0.4 | 0.5 | 3.87 | 18.2 | 1.678 | 28.0 | 0.8 | 139.0 | 4.5 | 101.0 | 21.0 |
| 76 | 0.5 | 0.8 | 3.56 | 15.3 | 0.53 | 23.0 | 0.7 | 141.0 | 3.8 | 102.0 | 23.0 |
| 77 | 0.6 | 0.7 | 4.21 | 18.3 | 0.4221 | 24.0 | 0.6 | 138.0 | 3.9 | 101.0 | 21.0 |
| 78 | 0.9 | 0.6 | 3.89 | 20.1 | 0.762 | 22.0 | 0.6 | 138.0 | 4.0 | 103.0 | 24.0 |
| 79 | 0.7 | 0.4 | 3.56 | 19.5 | 1.1 | 18.0 | 1.1 | 139.0 | 3.6 | 104.0 | 25.0 |
| 80 | 0.8 | 0.5 | 3.41 | 16.5 | 1.46 | 19.0 | 1.1 | 141.0 | 3.7 | 100.0 | 26.0 |

Source: Author's Field Work, 2023.

**Data from Measurement (Control)**

| S/N | Weight | Height | SystP | DiastP | HbA1C |
|---|---|---|---|---|---|
| 1. | 76.0 | 170.0 | 114.0 | 60.0 | 5.2 |
| 2. | 77.0 | 170.0 | 120.0 | 98.0 | 5.4 |
| 3. | 74.0 | 178.0 | 116.0 | 82.0 | 6.0 |
| 4. | 68.0 | 183.0 | 114.0 | 73.0 | 5.5 |
| 5. | 60.0 | 165.0 | 120.0 | 86.0 | 6.0 |
| 6. | 71.0 | 160.0 | 116.0 | 73.0 | 4.5 |
| 7. | 73.0 | 170.0 | 138.0 | 75.0 | 6.1 |
| 8. | 58.0 | 171.0 | 120.0 | 80.0 | 5.4 |
| 9. | 81.0 | 170.0 | 126.0 | 83.0 | 4.6 |
| 10. | 64.0 | 154.0 | 121.0 | 86.0 | 4.9 |
| 11. | 64.0 | 164.0 | 122.0 | 69.0 | 5.7 |
| 12. | 57.0 | 177.0 | 128.0 | 73.0 | 5.3 |
| 13. | 79.0 | 169.0 | 118.0 | 78.0 | 5.1 |
| 14. | 69.0 | 172.0 | 123.0 | 93.0 | 5.3 |
| 15. | 61.0 | 178.0 | 118.0 | 84.0 | 5.6 |

| | | | | | |
|---|---|---|---|---|---|
| 16. | 62.0 | 161.0 | 121.0 | 67.0 | 5.3 |
| 17. | 58.0 | 164.0 | 122.0 | 73.0 | 4.8 |
| 18. | 80.0 | 168.0 | 122.0 | 75.0 | 4.9 |
| 19. | 61.0 | 172.0 | 121.0 | 79.0 | 5.3 |
| 20. | 74.0 | 159.0 | 119.0 | 63.0 | 4.8 |
| 21. | 65.0 | 169.0 | 130.0 | 92.0 | 5.3 |
| 22. | 52.0 | 158.0 | 125.0 | 85.0 | 5.3 |
| 23. | 86.0 | 163.0 | 137.0 | 84.0 | 5.0 |
| 24. | 91.0 | 189.0 | 127.0 | 99.0 | 5.2 |
| 25. | 76.0 | 164.0 | 120.0 | 80.0 | 5.7 |
| 26. | 59.0 | 172.0 | 131.0 | 91.0 | 4.5 |
| 27. | 59.0 | 170.0 | 131.0 | 86.0 | 4.6 |
| 28. | 60.0 | 175.0 | 122.0 | 72.0 | 5.0 |
| 29. | 70.0 | 177.0 | 131.0 | 82.0 | 4.5 |
| 30. | 70.0 | 186.0 | 120.0 | 97.0 | 4.9 |
| 31. | 77.0 | 170.0 | 120.0 | 98.0 | 5.4 |
| 32. | 74.0 | 178.0 | 116.0 | 82.0 | 6.0 |
| 33. | 68.0 | 183.0 | 114.0 | 73.0 | 5.5 |
| 34. | 60.0 | 165.0 | 120.0 | 86.0 | 6.0 |

35. 71.0 160.0 116.0 73.0 4.5

36. 73.0 170.0 122.0 75.0 6.1

37. 58.0 171.0 120.0 80.0 5.4

38. 81.0 170.0 126.0 83.0 4.6

39. 64.0 154.0 121.0 86.0 4.9

40. 64.0 164.0 122.0 69.0 5.7

41. 57.0 177.0 128.0 73.0 5.3

42. 79.0 169.0 118.0 78.0 5.1

43. 69.0 172.0 123.0 93.0 5.3

44. 61.0 178.0 126.0 84.0 5.6

45. 62.0 161.0 121.0 67.0 5.3

46. 58.0 164.0 122.0 73.0 4.8

47. 80.0 168.0 122.0 75.0 4.9

48. 61.0 172.0 121.0 79.0 5.3

49. 76.0 169.0 120.0 80.0 5.7

50. 70.0 169.0 122.0 81.0 5.2

51. 64.0 154.0 121.0 86.0 4.9

52. 64.0 164.0 122.0 69.0 5.7

53. 57.0 177.0 128.0 73.0 5.3

54. 79.0 169.0 118.0 78.0 5.1

55. 69.0 172.0 123.0 93.0 5.3

56. 61.0 178.0 126.0 84.0 5.6

57. 62.0 161.0 121.0 67.0 5.3

58. 58.0 164.0 122.0 73.0 4.8

59. 80.0 168.0 122.0 75.0 4.9

60. 61.0 172.0 121.0 79.0 5.3

61. 76.0 169.0 120.0 80.0 5.7

62. 70.0 169.0 122.0 81.0 5.2

63. 79.0 169.0 118.0 78.0 5.1

64. 69.0 172.0 123.0 93.0 5.3

65. 61.0 178.0 126.0 84.0 5.6

66. 62.0 161.0 121.0 67.0 5.3

67. 58.0 164.0 122.0 73.0 4.8

68. 80.0 168.0 122.0 75.0 4.9

69. 61.0 172.0 121.0 79.0 5.3

70. 76.0 169.0 120.0 80.0 5.7

71. 70.0 169.0 122.0 81.0 5.2

72. 70.0 169.0 122.0 81.0 5.2

| | | | | | |
|---|---|---|---|---|---|
| 73. | 79.0 | 169.0 | 118.0 | 78.0 | 5.1 |
| 74. | 69.0 | 172.0 | 123.0 | 93.0 | 5.3 |
| 75. | 61.0 | 178.0 | 126.0 | 84.0 | 5.6 |
| 76. | 62.0 | 161.0 | 121.0 | 67.0 | 5.3 |
| 77. | 58.0 | 164.0 | 122.0 | 73.0 | 4.8 |
| 78. | 80.0 | 168.0 | 122.0 | 75.0 | 4.9 |
| 79. | 61.0 | 172.0 | 121.0 | 79.0 | 5.3 |
| 80. | 76.0 | 169.0 | 120.0 | 80.0 | 5.7 |
| 81. | 70.0 | 169.0 | 122.0 | 81.0 | 5.2 |
| 82. | 69.0 | 172.0 | 123.0 | 93.0 | 5.3 |
| 83. | 61.0 | 178.0 | 126.0 | 84.0 | 5.6 |
| 84. | 62.0 | 161.0 | 121.0 | 67.0 | 5.3 |
| 85. | 58.0 | 164.0 | 122.0 | 73.0 | 4.8 |

Source: Author's Field Work, 2023.

**Data from Measurement (Case)**

| S/N | Weight | Height | SystP | DiastP | HbA1C |
|---|---|---|---|---|---|
| 1. | 61.0 | 178.0 | 126.0 | 84.0 | 5.6 |
| 2. | 62.0 | 161.0 | 121.0 | 67.0 | 5.3 |
| 3. | 58.0 | 164.0 | 122.0 | 73.0 | 4.8 |
| 4. | 80.0 | 168.0 | 122.0 | 75.0 | 4.9 |
| 5. | 77.0 | 170.0 | 120.0 | 98.0 | 5.4 |
| 6. | 74.0 | 178.0 | 116.0 | 82.0 | 6.0 |
| 7. | 68.0 | 183.0 | 114.0 | 73.0 | 5.5 |
| 8. | 60.0 | 165.0 | 120.0 | 86.0 | 6.0 |
| 9. | 71.0 | 160.0 | 116.0 | 73.0 | 4.5 |
| 10. | 76.0 | 168.0 | 120.0 | 80.0 | 5.2 |
| 11. | 82.0 | 162.0 | 122.0 | 78.0 | 4.8 |
| 12. | 67.0 | 158.0 | 119.0 | 82.0 | 4.9 |
| 13. | 59.0 | 159.0 | 118.0 | 67.0 | 5.0 |
| 14. | 62.0 | 168.0 | 122.0 | 81.0 | 4.2 |
| 15. | 59.0 | 167.0 | 123.0 | 81.0 | 5.3 |

| | | | | | |
|---|---|---|---|---|---|
| 16. | 70.0 | 171.0 | 120.0 | 80.0 | 5.2 |
| 17. | 69.0 | 172.0 | 132.0 | 65.0 | 5.1 |
| 18. | 68.0 | 180.0 | 131.0 | 67.0 | 5.0 |
| 19. | 69.0 | 169.0 | 118.0 | 78.0 | 5.1 |
| 20. | 74.0 | 172.0 | 123.0 | 93.0 | 5.3 |
| 21. | 75.0 | 178.0 | 126.0 | 84.0 | 5.6 |
| 22. | 72.0 | 161.0 | 121.0 | 67.0 | 5.3 |
| 23. | 69.0 | 164.0 | 122.0 | 73.0 | 4.8 |
| 24. | 68.0 | 168.0 | 122.0 | 75.0 | 4.9 |
| 25. | 79.0 | 172.0 | 121.0 | 79.0 | 5.3 |
| 26. | 76.0 | 169.0 | 120.0 | 80.0 | 5.7 |
| 27. | 76.0 | 169.0 | 122.0 | 81.0 | 5.2 |
| 28. | 68.0 | 172.0 | 123.0 | 93.0 | 5.3 |
| 29. | 66.0 | 178.0 | 126.0 | 84.0 | 5.6 |
| 30. | 69.0 | 161.0 | 121.0 | 67.0 | 5.3 |
| 31. | 68.0 | 164.0 | 122.0 | 73.0 | 4.8 |
| 32. | 78.0 | 178.0 | 126.0 | 84.0 | 5.6 |
| 33. | 77.0 | 161.0 | 121.0 | 67.0 | 5.3 |
| 34. | 69.0 | 164.0 | 122.0 | 73.0 | 4.8 |

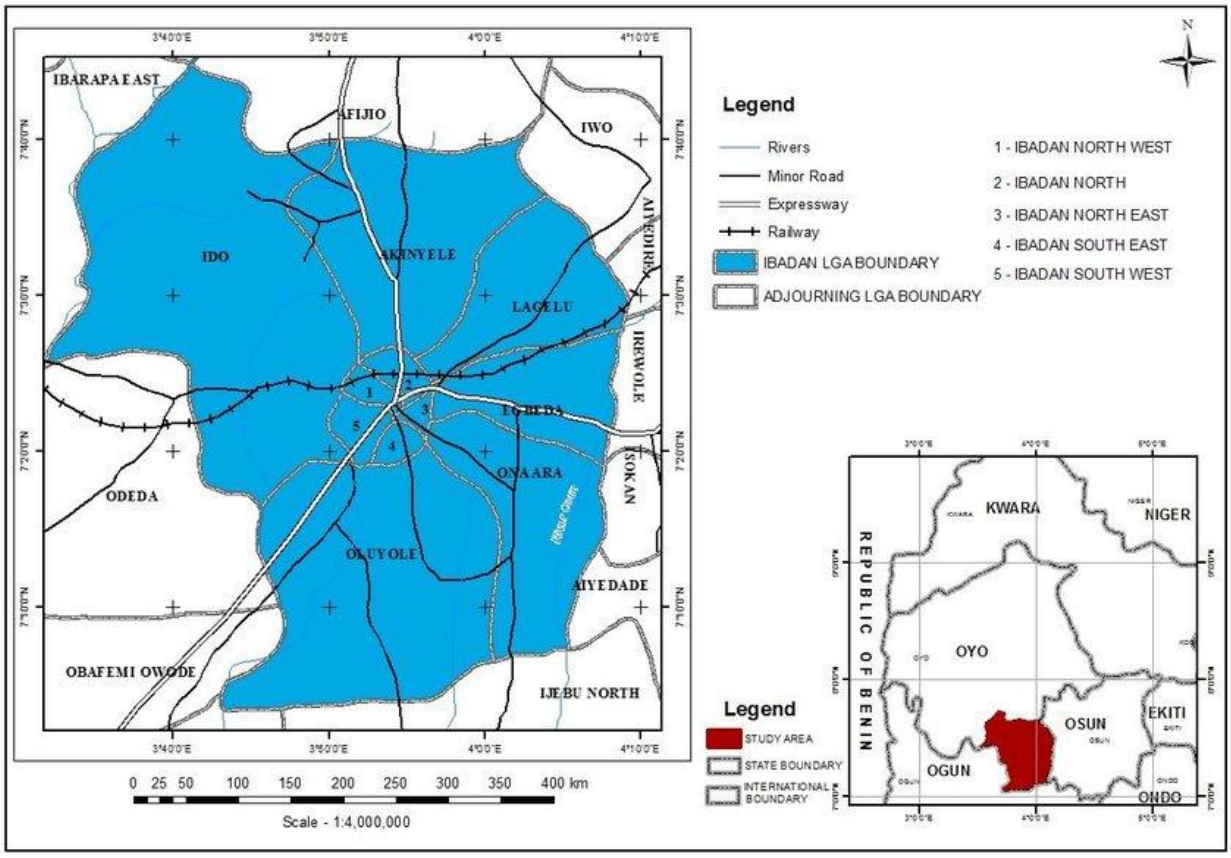
| | | | | | |
|---|---|---|---|---|---|
| 35. | 71.0 | 170.0 | 119.0 | 79.0 | 4.9 |
| 36. | 60.0 | 173.0 | 116.0 | 75.0 | 5.0 |
| 37. | 76.0 | 189.0 | 123.0 | 80.0 | 4.8 |
| 38. | 80.0 | 192.0 | 121.0 | 79.0 | 5.2 |
| 39. | 91.0 | 189.0 | 127.0 | 99.0 | 5.2 |
| 40. | 76.0 | 164.0 | 120.0 | 80.0 | 5.7 |
| 41. | 59.0 | 172.0 | 131.0 | 91.0 | 4.5 |
| 42. | 59.0 | 170.0 | 131.0 | 86.0 | 4.6 |
| 43. | 60.0 | 175.0 | 122.0 | 72.0 | 5.0 |
| 44. | 70.0 | 177.0 | 131.0 | 82.0 | 4.5 |
| 45. | 70.0 | 186.0 | 120.0 | 97.0 | 4.9 |
| 46. | 77.0 | 170.0 | 120.0 | 98.0 | 5.4 |
| 47. | 74.0 | 178.0 | 116.0 | 82.0 | 6.0 |
| 48. | 68.0 | 183.0 | 114.0 | 73.0 | 5.5 |
| 49. | 60.0 | 165.0 | 120.0 | 86.0 | 5.1 |
| 50. | 67.0 | 168.0 | 122.0 | 80.0 | 4.9 |
| 51. | 72.0 | 175.0 | 125.0 | 83.0 | 5.2 |
| 52. | 68.0 | 165.0 | 122.0 | 80.0 | 5.1 |
| 53. | 59.0 | 172.0 | 129.0 | 82.0 | 4.9 |

| | | | | | |
|---|---|---|---|---|---|
| 54. | 74.0 | 178.0 | 116.0 | 82.0 | 6.0 |
| 55. | 68.0 | 183.0 | 114.0 | 73.0 | 5.5 |
| 56. | 60.0 | 165.0 | 120.0 | 86.0 | 5.1 |
| 57. | 67.0 | 168.0 | 122.0 | 80.0 | 4.9 |
| 58. | 72.0 | 175.0 | 125.0 | 83.0 | 5.2 |
| 59. | 58.0 | 164.0 | 122.0 | 73.0 | 4.8 |
| 60. | 80.0 | 170.0 | 122.0 | 75.0 | 4.9 |
| 61. | 77.0 | 170.0 | 120.0 | 98.0 | 5.4 |
| 62. | 74.0 | 178.0 | 116.0 | 82.0 | 6.0 |
| 63. | 68.0 | 183.0 | 114.0 | 73.0 | 5.5 |
| 64. | 60.0 | 165.0 | 120.0 | 86.0 | 6.0 |
| 65. | 71.0 | 160.0 | 116.0 | 73.0 | 4.5 |
| 66. | 76.0 | 168.0 | 120.0 | 80.0 | 5.2 |
| 67. | 82.0 | 162.0 | 122.0 | 78.0 | 4.8 |
| 68. | 67.0 | 158.0 | 119.0 | 82.0 | 4.9 |
| 69. | 62.0 | 169.0 | 118.0 | 67.0 | 5.0 |
| 70. | 62.0 | 161.0 | 121.0 | 67.0 | 5.3 |
| 71. | 58.0 | 164.0 | 122.0 | 73.0 | 4.8 |
| 72. | 80.0 | 168.0 | 122.0 | 75.0 | 4.9 |

| | | | | | |
|---|---|---|---|---|---|
| 73. | 77.0 | 170.0 | 120.0 | 98.0 | 5.4 |
| 74. | 74.0 | 178.0 | 116.0 | 82.0 | 6.0 |
| 75. | 83.0 | 183.0 | 114.0 | 73.0 | 5.5 |
| 76. | 60.0 | 165.0 | 120.0 | 86.0 | 6.0 |
| 77. | 71.0 | 171.0 | 116.0 | 73.0 | 4.5 |
| 78. | 76.0 | 168.0 | 120.0 | 80.0 | 5.2 |
| 79. | 82.0 | 170.0 | 122.0 | 78.0 | 4.8 |
| 80. | 72.0 | 168.0 | 119.0 | 75.0 | 5.0 |

Source: Author's Field Work, 2023.

Map of Ibadan Metropolis Showing Local Government Areas (Inset: Oyo State Showing the Study Area).




Source: Office of Surveyor General of the Federation (OSGOF, 2014)

Study was carried out at Ibadan North, Ibadan Northwest, Lagelu and Oluyole local government areas.

## Bio-data

**A. Personal Data:**

| | |
|---|---|
| **1. Full Name:** | OGUNLEYE, Temitope David<br>55/56, Adeniyi Layout, Iyana Church,<br>Ibadan<br>topdar2k2@yahoo.com. |
| **2.** Date and Place of Birth | 21st, June 1983, Lagos |
| **3.** Nationality | Nigerian. |
| **4.** State of Origin | Ekiti |
| **5.** Name and Address of Next of Kin | Mrs OGUNLEYE, Olujoke Olajumoke<br>55/56, Adeniyi Layout, Iyana Church,<br>Ibadan |

**2. Educational Background**

**Educational Institutions Attended with Dates and Qualification**

**School Attended** **Date**

**PhD Biology (Immunology) in view.** **2019-2023**
Lead City University, Oyo state, Nigeria.
Subjects studied include Molecular Immunology, Genomics and Methodology, Research Methodology

**Master of Science (M.Sc.) in Chemical Pathology and Immunology.** **2012-2014**
University of Ibadan, Ibadan, Oyo state, Nigeria. Subjects studied include Clinical Chemistry, Immunology, Reproductive Endocrinology, Biostatistics, Laboratory techniques.

**Bachelor of Medical Laboratory Science (BMLS).** **2004-2009**
Ladoke Akintola University of Technology, Ogbomosho, Oyo state Nigeria.
**Subjects Studied Include**: Biochemistry, Hematology, Cell and Molecular Biology, Genetics, Histopathology, Medical Microbiology, Blood group serology. Laboratory techniques.

**West African secondary school certificate examination** (WASSCE) **1995-2001**
Comprehensive High School, Alapere, Ketu, Lagos state, Nigeria

## 3. Work Experience **Date**

**University College Hospital, Chemical Pathology Department, Ibadan**
*Assistant Director Medical Laboratory Scientist.* (2022-Till Date)

Job Description

- Assigning responsibilities to and supervising junior colleagues.
- Ensuring maintenance of quality control and standards in service laboratories.
- Collating and reviewing annual reports.
- Taking charge of a branch
- Assisting in employment and ensuring adequate and continuous training of Medical Laboratory Personnel.
- Assisting in the general administration of the Department

**International Institute for Tropical Agriculture (IITA)**
National Food Consumption and Micronutrient Survey. (September to November 2021)
*Laboratorian and Data Manager* (Consultancy/Contract Job)

Job Description

- National Data management.
- Handling of biological specimens (Blood, Urine and Stool).
- Taking inventory of all the samples collected on the field.
- Creation of National catalog for various analytes using MS excel.
- Arrangement of biological samples for the purpose of shipment and analysis.
- Maintenance of cold chain of biological samples.

- Report activities to the Zonal coordinator and National Biomarker lead

**International Institute for Tropical Agriculture (IITA)**
National Food Consumption and Micronutrient Survey. (August to September 2021)
Modified Relative Dose Response (MRDR) Survey.
*Field Laboratorian* (Consultancy/Contract Job

Job Description

- Mobilization of selected respondent for the survey
- Confirming the age of the respondents through the national identification card and birth certificate
- Confirmation of the pregnancy status of the participants.
- Checking the body temperature of the respondents.
- Administration of Vitamin A analog to the respondents
- Administration of high fat diet to the respondents
- Assisting the Phlebotomist in blood sample collection
- Setting up a field laboratory for sample processing
- Maintenance of cold chain of samples and analog
- Taking inventory of materials and supplies.
- Report activities on the field to the Zonal Coordinator



**International Institute for Tropical Agriculture (IITA)**
National Food Consumption and Micronutrient Survey. (February to June 2021)
*Field Laboratorian* (Consultancy/Contract Job).

Job Description

- Set up and sanitize field laboratory.
- Assist in the taking of anthropometry measurements.

- Assist in phlebotomy process.
- Process collected samples including centrifugation and aliquoting samples.
- Analyze samples using point-of-care machine and rapid diagnostic test kits while adhering strictly to the SOP.
- Identification of stool parasites through microscopy.
- Pack and transport biological samples to a temporary storage facility.
- Maintenance of cold chain of samples using TMT (temperature monitoring tools).
- Record all data and results in specified forms paper with accuracy.
- Record (Upload) all field data on ComCare.
- Always keep the workstation well-organized.
- Adhere to all relevant health and safety standards while working.

**Nigeria Centre for Disease Control**
Short term consultancy on the Surveillance, Outbreak Response Management and Analysis System (SORMAS), for Oyo state Laboratories assaying for COVID-19.
*SORMAS Data Clerk* (Consultancy/Contract Job). 2020-2021

Job Description

- Transfer all COVID 19, Lassa fever and other priority diseases data (clinical and laboratory data) into the SORMAS platform.
- Daily follow up with result of all COVID 19, Lassa fever and other priority diseases case data sent for testing.
- Liaise with the lab managers to ensure prompt release of result and update on SORMAS.
- Real time update of SORMAS with result of COVID 19, Lassa Fever and other priority diseases samples after testing.
- Send daily notification on status of sample testing.

- Follow up with treatment Centre clinicians to ensure completion of COVID 19 and LF case management form.
- Compile and upload Case management forms into SORMAS
- Verify all the treatment centre COVID 19 and Lassa fever data on the SORMAS platform by comparing it to source documents (i.e., Lassa fever case management form, COVID 19 case management form and IDSR 001B)
- Retrieve data from the SORMAS platform as requested.
- Sort and organize paper forms (Lassa fever case management form, COVID-19 case management form and IDSR 001B) after entering data into the SORMAS platform to ensure it is not lost.
- Send details of any record in the lab without case data in SORMAS platform to the NCDC Surveillance Support Officer to follow up with the LGA DSNO.
- Send weekly report of COVID 19 and Lassa fever cases in the treatment centre to the COVID-19/Lassa fever TWG.
- Perform other tasks assigned.

**Emergency Operation Centre, Oyo State on COVID-19 Response.**
Short term volunteer on the Outbreak Response on COVID -19 (March-May, 2020).
*Secretary, Data manager and Sample collector, Laboratory Pillar.*

Job Description

- Assisting the Laboratory Pillar lead in the coordination of Covid sample collection across the state.
- Drawing up daily work schedule for sample collection and transfer of samples to the laboratories for analysis
- Daily presentation of Laboratory Pillar activities at the Emergency Operation Centre, Oyo State on COVID-19 Response.

- Collection and transfer of samples to the Laboratory.
- Taking daily inventory of supplies.

**University College Hospital, Chemical Pathology Department, Ibadan**
*Chief Medical Laboratory Scientist.* (2019-2021)

Job Description

- Analysis of biological samples (Blood, urine, cerebrospinal fluid, stool, Ascitic fluid, etc.) for the purpose of diagnosis, treatment, monitoring, prognosis, and research.
- Carry out routine internal quality control.
- Coordinating the duties of all the Medical/Laboratory Technicians and assigning other responsibilities might arise from time to time.
- Procuring laboratory equipment and chemical reagents
- Maintaining technical data and records in the research and service laboratory and assuming total responsibility for all laboratory technicalities.

**University College Hospital, Public-Private Partnership Laboratory, UCH Ibadan**
*Principal Medical Laboratory Scientist* (2016-2019)

Job Description

- Analysis of biological samples (Blood, urine, cerebrospinal fluid, stool, Ascitic fluid, etc.) for the purpose of diagnosis, treatment, monitoring, prognosis, .and research.
- Assisting in the coordination of internal quality control activities.
- Assisting in supervising and coordinating the activities of junior officers in the various Units of the laboratory.
- Taking charge of a specialized aspect of a research project.
- Training of junior officers on the automated systems in the Laboratory

**University College Hospital, Public-Private Partnership Laboratory, UCH Ibadan**

*Medical Laboratory Scientist* 1 (2012-2015)

Job Description

- Analysis of biological samples (Blood, urine, cerebrospinal fluid, stool, Ascitic fluid, etc.) for the purpose of diagnosis, treatment, monitoring, prognosis, and research.
- Maintaining and carrying out minor repairs of laboratory equipment.
- Identifying medical equipment and supplies in the Medical Store.
- Training of junior officers on the automated systems in the Laboratory
- Assisting in the training and supervision of junior staff in the laboratory

**4. Awards and Fellowships (If any)**

African Federation of Clinical Chemistry (AFCC) travel grant, to attend and present at the IFCC World Lab, Congress, Seoul Awarded to < 5% of applicants.

**2022**

American Association for Clinical Chemistry (AACC) travel grant award, to attend and present at the AACC conference, San Diego California. Awarded to < 5% of applicants.

**2017**

International Federation of Clinical Chemistry and lab. Medicine travel grant award, to attend and present at the World-Lab conference at Durban, South Africa, Awarded to < 20% of applicants.

**2017**

Roche South Africa/ISN Nigeria travel grant to train at Roche Scientific campus, Randburg, South Africa, on COBAS C311, and COBAS 6000, basic and advance operation, and software application.

**2015**

Best student in Chemistry. Comprehensive High School, Alapere Ketu, Lagos State, Nigeria.

**2001**

Student with the highest number of distinctions in 2001 West African secondary school certificate examination at Comprehensive High School, Alapere Ketu, Lagos state, Nigeria

**2001**

**5. Membership of Academic Professional Bodies**

Association of Medical Laboratory Scientist of Nigeria (AMLSN).

Association of Clinical Chemists of Nigeria (ACCN).

American Association for Clinical Chemistry and Laboratory Medicine (AACC).

International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

Nigeria Society for Immunology (NSI)

Young Scientist forum of ACCN

## 6. Publication

**Ogunleye T.D**, Adelakun A.A, Arinola O.G. The effect of Pneumococcal vaccination on acute-phase reactants and trace elements in sickle cell children. *Journal of Clinical Chemistry and Laboratory Medicine* 2017; 55, pp S1-S1121

**Ogunleye T.D**, Disu E.A, Adelakun A.A, Ajani O.F, Rahamon S.K, Arinola O.G. Acute-phase reactants, essential trace elements and some hematological parameters in Nigerian children with steady state sickle cell disorder. *Journal of Medicine in the Tropics* (2015) 17:2:1-4

Ayodele Adelakun, Olumide Ajani, **Temitope Ogunleye**, Elizabeth Disu, Ayokulehin Kosoko and Ganiyu Arinola. Respiratory Burst Enzymes and Oxidant-antioxidant Status in Nigerian Children with Sickle Cell Disease. *British Biotechnology Journal* 4(3): 270-278, 2014

Ajani O. Faith, Adelakun Ayodele, **Ogunleye D. Temitope**, Disu Elizabeth, Olaniyi John,Rahamon K. Sheu, Arinola O. Ganiyu. Increased IgE level in Nigerian sickle cell disease children: Implication for severity of allergic reactions. *Journal of Applied Hematology* Vol. 4 • Issue 4 • October-December 2013.

**Major conferences with abstracts accepted and presented.**

Prevalence of hepatitis B virus and hepatitis C virus co-infection in both apparently healthy adults and suspected viral hepatitis patients of the chemical pathology laboratory, university college hospital, Ibadan. A digital postal presentation at the IFCC World Lab Congress, Seoul. **2022**

Prevalence of hepatitis B viral infection in apparently healthy adult clients of public private partnership laboratory, University college hospital, Ibadan Nigeria, A postal presentation at the American Association for Clinical Chemistry, (AACC) conference Chicago, Illinois. **2018**.

Comparative study of liver enzymes in uncomplicated type 2 diabetics and apparently healthy individuals at the University College Hospital Ibadan, Nigeria. A postal presentation at the American Association for Clinical Chemistry (AACC) conference. San Diego, California, USA **2017**

The effect of pneumococcal vaccination on acute phase reactants and trace elements in sickle cell disease children. A postal presentation at the World-Lab conference at Durban, South Africa of the International Federation of clinical chemistry and lab. Medicine. **2017.**

Signature Date

**The University Compliance Certification**

This is to certify that the thesis of **Temitope David OGUNLEYE,** with matriculation number **LCU/PG/001442**, In the Department of Biological Science, Faculty of Natural and Applied Sciences, Lead City University, Ibadan, Nigeria is in full compliance with the approved University Format and Style.

Signature Date