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*Georgia State University*

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doi: <https://doi.org/10.57709/32740384>

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The Effect of Ketone on  $\beta$ -aminopropionitrile-induced Vascular Remodeling

by

Abdulgafar D. Ibrahim

Under the Direction of Ping Song, Ph.D.

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of  
Master of Interdisciplinary Studies  
in the Institute for Biomedical Sciences  
Georgia State University

2022

## ABSTRACT

**Background:** Aortic aneurysms and dissections (AD) are common in aging populations, and their development is tightly associated with vascular inflammation. Aortic dissection and rupture are associated with high mortality. Currently, there is no effective drug treatment for AD progression and rupture except surgical treatment. Although ketone bodies have an anti-inflammation effect, it remains unclear whether ketone restrains AD and the risk of rupture.

**Methods:** C57BL/6J mouse underwent  $\beta$ -aminopropionitrile (BAPN) treatment with drinking water for 28 days, followed by angiotensin II (Ang II) mini-pump implantation for 3 days to induce AD. Ketone-ester (KE) was administered in drinking water starting at 17 days after initiation of BAPN treatment. There were four groups: Sham, BAPN+Ang II, BAPN+Ang II+KE 20 g/L, and BAPN+Ang II+KE 50 g/L. The blood ketone level was monitored by a Precision Xtra meter. Ultrasound was employed to measure the aorta strain.

**Results:** KE treatment (both 20 g/L and 50 g/L) reduced the incidence of both thoracic aortic dissection and abdominal aortic dissection. KE at 50 g/L increased the survival rate of BAPN plus AngII-treated mice. KE treatment did not reverse the Ang II-induced aortic stiffness demonstrated by reduced aorta strain. BAPN and KE did not affect mice weights, but Ang II slightly reduced the mouse body weight. BAPN and KE treatment had no effect on water consumption. These results suggest that ketone appears to decrease aortic dissection and risk of rupture and provides a potential therapeutic strategy for aortic dissection.

**INDEX WORDS:** Aortic dissection; Aorta stiffness; BAPN; Angiotensin II; Ketone

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2022

# The Effect of Ketone on $\beta$ -aminopropionitrile-induced Vascular Remodeling

by

Abdulgafar D. Ibrahim

Committee Chair: Ping Song

Committee: Chunying Li

Electronic Version Approved:

Office of Academic Assistance – Graduate Programs

Institute for Biomedical Sciences

Georgia State University

December 2022

## ACKNOWLEDGEMENTS

First, I would like to express my sincere thanks to my thesis mentor, Dr. Ping Song, for his continued support, advice, and valuable scientific expertise. I would also like to thank Dr. Yang Wu, who is an immediate mentor, for teaching me experimental techniques, data collection, data analysis and interpretation. My great thanks also go to my committee member, Dr. Chunying Li, for his valuable advice and guidance on the thesis defense and revision. Next, I would like to thank all the past and present members in Dr. Song's lab, including Sanjiv Shrestha. I have had such a wonderful time to work with you. I would like to give special thanks to the lab managers. Without your great work, the lab could not run so smoothly.

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## 1 INTRODUCTION

The vascular system consists of arteries (carrying the oxygenated blood), capillaries (the level at which there is an exchange of blood nutrients, oxygen, and waste products), and veins (receiving the deoxygenated blood). These are important for tissue homeostasis through the provision of oxygen and nutrients, and the removal of waste products. (1). The vascular smooth muscle extracellular matrix that consists of collagen and elastin is important for maintaining mechanical integrity. Lysyl oxidase (LOX) and lysyl oxidase-like 1-4 (LOXL1-4) enzymes play a key role in the remodeling of vascular smooth muscle extracellular matrix (ECM). These enzymes are important for connecting the elastin with the collagens in the ECM. The deficiency of these enzymes can result in disrupted elastin and collagen cross-links. (1,2,3).

$\beta$ -aminopropionitrile (BAPN) and penicillamine are potent inhibitors of lysyl oxidase (LOX). (5). This results in a deficiency of enzymes and a lack of cross-linking between the elastin and collagen in the smooth muscle extracellular matrix to form desmsine. BAPN can also induce systemic inflammation by acting on the immune system. This enables an inflammatory response and causes vascular damage. (4,5). Many studies have demonstrated the use of BAPN with angiotensin II (AngII) Infusion to promote aortic damage. However, the use of BAPN without angiotensin II infusion can also induce aortic damage formation. (4)

Aortic diseases are life-threatening and associated with high mortality. The cause of most of these is unknown, but the risk increases with high blood pressure and inflammation. The persistent exposure of vascular endothelium to inflammatory stress/chemokines facilitates the development of aortic aneurysms and dissections. (2,4).

The aortic smooth muscle cells contract to regulate the lumen size based on blood pressure. However, increased blood pressure and inflammatory stress promote dysfunction of the vascular endothelium. Aortic aneurysms are defined as the increased luminal size of the aorta, associated with a risk of uncontrolled bleeding due to rupture of the aorta. Aortic dissections are defined as the bleeding into the medial layers of the aorta resulting in organ dysfunction. (2,4).

Ketone bodies (acetoacetate,  $\beta$ -hydroxybutyrate, acetone) are produced by hepatic mitochondria from acetyl CoA and transported to other tissues like the heart, brain, and muscles for energy production when fatty acids and carbohydrates are not available (During fasting or strenuous exercise). Acetoacetate and  $\beta$ -hydroxybutyrate are the major ketone bodies used by the cardiovascular system. The ketone body, especially  $\beta$ -hydroxybutyrate ( $\beta$ -OHB) has been found in cardiovascular disease metabolism as an energy source. This is an important adaptive response to stress during the pathological progression of the disease. It has also been demonstrated to decrease the production of reactive oxygen species and autophagy. The increased levels of  $\beta$ -OHB before cardiovascular injury result in reduced damage to the system in an animal. (6,7,8). AAD (abdominal aortic dissection) may be associated with high energy consumption and limited ability to store ATP, there is a need for a continuous supply of efficient exogenous substrate for energy production. (9,10). It has been shown that a prolonged caloric restriction decreases inflammatory response, however, the effect of Ketones and other related energy producing substrates on the immune system is not well understood. (11). The aim of this study is to test the anti-inflammatory function of  $\beta$ -OHB in the prevention of aortic aneurysm and dissection.

## 2 METHOD AND MATERIALS

### 2.1 Experimental Animal

Five weeks old wild-type C57BL/6J mice were used with each weighing an average of 18 g. The animals were all maintained under a light/dark cycle (12/12 h). The mice ate and drank according to the experimental design. Georgia State University's Animal Care and Use Committee approved this study.

### 2.2 Reagents

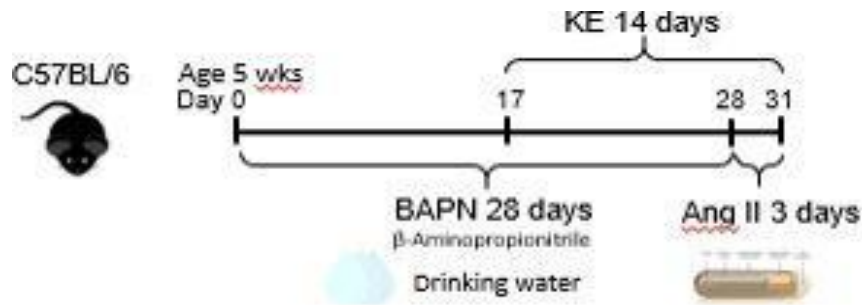
$\beta$ -aminopropionitrile (BAPN, Product number; A0796), and Ketone-ester (D-BHB 1-3 butanediol monoester) purchased from TCI and ketoneaid in the United States respectively.

### 2.3 Animal Model

The animals were divided into two groups randomly, 10 in the control group and 35 in the model group. In the model group, BAPN at 3 g/L was added to the drinking water for 28 days (about 4 weeks). Body weight was measured every alternate day (2 days).

On the seventeen days of the study, 5 ml (about 0.17oz) per day per mouse of 20 g pure Ketone-ester (KE)/L (40 g/L drinking water to supply ketone), 20 g BW per mouse. 5 g KE/kg daily for 2 weeks. During the experiment, non-fasting  $\beta$ -OHB levels were periodically measured using a Precision Xtra meter. On the 28<sup>th</sup> day of the experiment, a subcutaneous infusion of Angiotensin II using an osmotic pump of 1000 ng/kg/min for 3 days (**Figure 1**).

The control group fed on the commercial feed (pellets) and drank autoclaved water throughout the research study.



**Figure 1: Scheme of animal treatment with BAPN, KE, and Ang II**

## 2.4 Echocardiography

The aorta vessel function was examined using Vevo 3100 echocardiography machine and an MS 550D probe (22-55 MHz) under anesthesia with 1% to 1.5% anesthetics (Isoflurane) in a 100% atmosphere gas chamber.

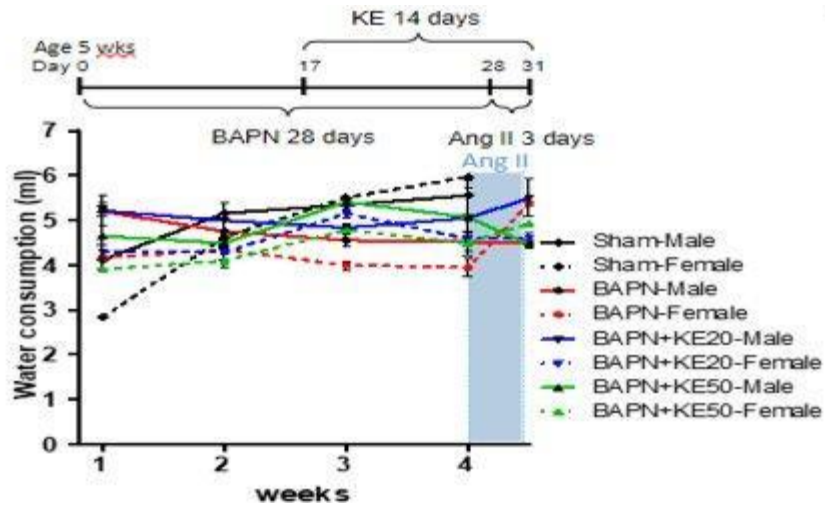
Mice were anesthetized and placed in a warm pad in a supine position. Warmed ultrasound gel was applied, and the probe was positioned to visualize the abdominal aorta at the level of the diaphragm and the branching of superior renal arteries.

M-mode tracings of aortic crossing view were recorded. Aortic Strain (Vascular Stiffness) was calculated using the radial strains formula;  $\varepsilon = (L - L_0)/L_0$ , the percent ratio of the systolic-diastolic diameter change, and diastolic diameter of the aorta. Doppler imaging was also carried out to determine the velocity of blood through the vessels.

## 3. RESULTS

### 3.1 Ketone-ester has no Effect on Animal Water Consumption

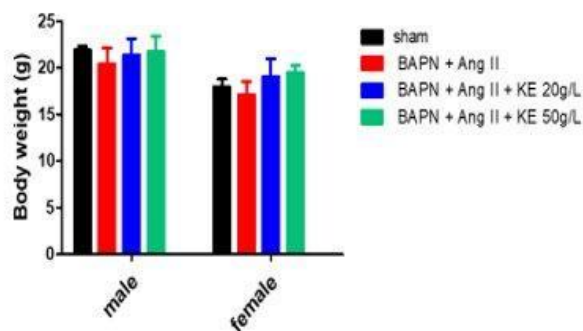
We first tested the effect of Ketone-Ester (KE) on water consumption of mice. As shown in **Figure 2**, KE at either 20 g/L or 50 g/L had no clear effect on the water consumption in mice.



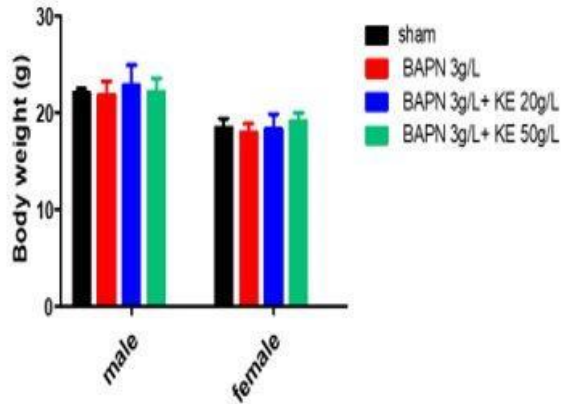
**Figure 2.** The effect of reagents on animal water consumption. Mice reduced water consumption after application of BAPN, water consumption was restored partially with KE (20 and 50 g KE) application in drinking water.

### 3.2. Effect of Ketone-ester on Body Weight

As shown in **Figure 3a**, BAPN and BAPN plus ketone-ester did not change the body weight of both male and female mice compared with the sham group. Although angiotensin II treatment slightly decreased the body weight of mice treated with BAPN, Ketone-Ester treatment blocked angiotensin II-mediated body weight reduction (**Figure 3b**).



a.

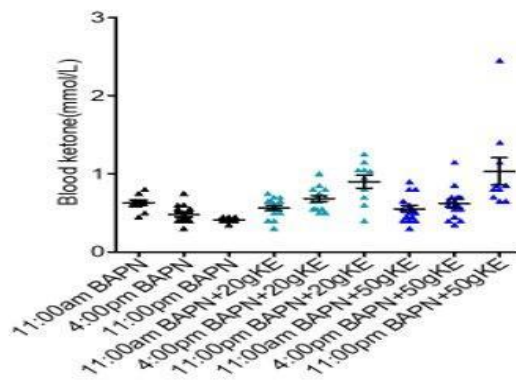


b.

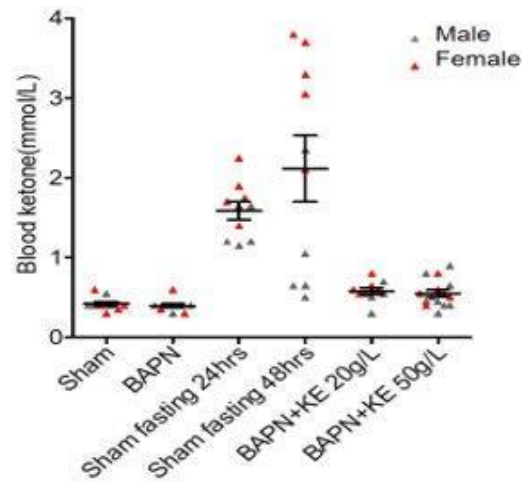
**Figure 3.** Body weight among mice groups. a. Body Weight at day 28 (just before Angiotensin II implantation). b. Body weight after Angiotensin II implantation (at day 31).

### 3.3 Blood Ketone Levels During Animal Experiments

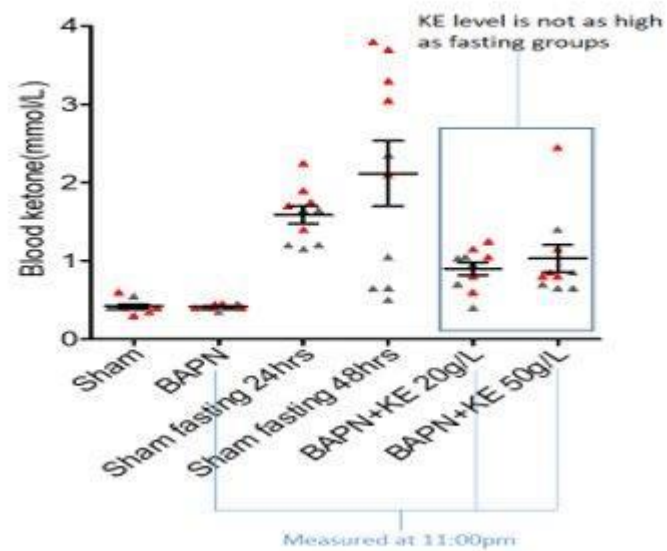
As previously reported, fasting clearly increased the blood ketone levels (**Figure 4b & c**). Blood ketone levels were increased after KE application (**Figure 4a-4c**), but only when the animal up took the water. Ketone levels tested during daytime in the 20 or 50 KE groups, especially in the morning around 11:00 am, did not show any different compared with the BAPN alone-treated group (**Figure 4b**). However, when the light was off, the ketone levels dramatically increased since the animals started to drink the KE-contained water (**Figure 4c**). Therefore, the ketone levels might be measured at least 2 hours after the light off.



a.



b.

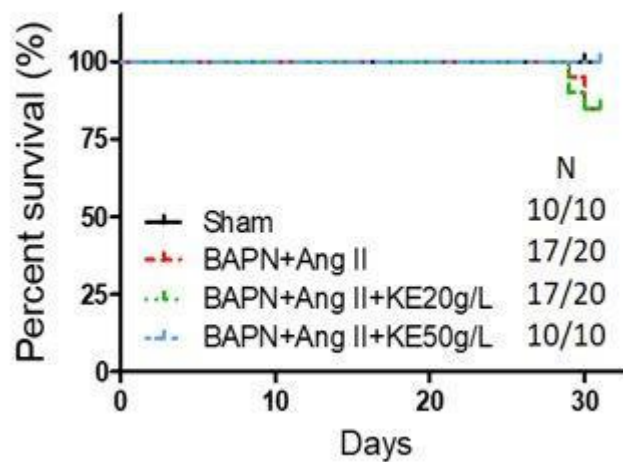


c.

**Figure 4.** Blood ketone levels. a: Blood ketone levels measured at three time points (11:00 am, 4:00 pm, and 11:00 pm) at age (5+3) weeks. b: Blood ketone level measured at daytime (about 11 am). c: Blood ketone level measured at night (about 11 pm).

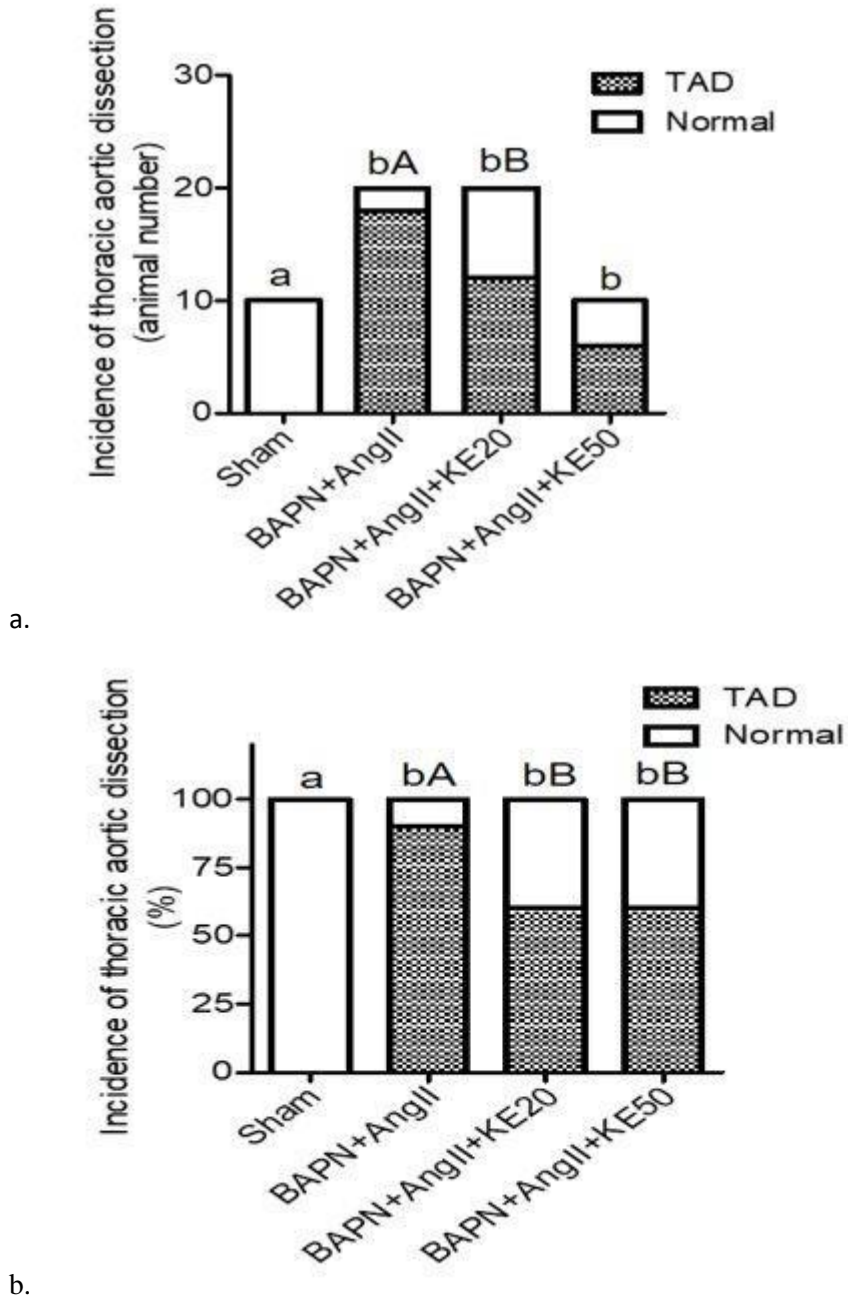
### 3.4 Survival Rate of Mice and Aortic Dissection

As shown in **Figure 5**, low dose of KE application (20 g/L) did not improve the survival rate compared to BAPN+Ang II group. Medium dose of KE application (50 g/L) improved survival rate: no mice died in the 50 g/L KE group. Both 20 g/L and 50 g/L KE dramatically decreased the number and percentage of thoracic aortic dissection (TAD) (**Figure 6a & b**). Furthermore, two dose KE also clearly decreased the number and percentage of abdominal aortic dissection (AAD) (**Figure 7a & b**).

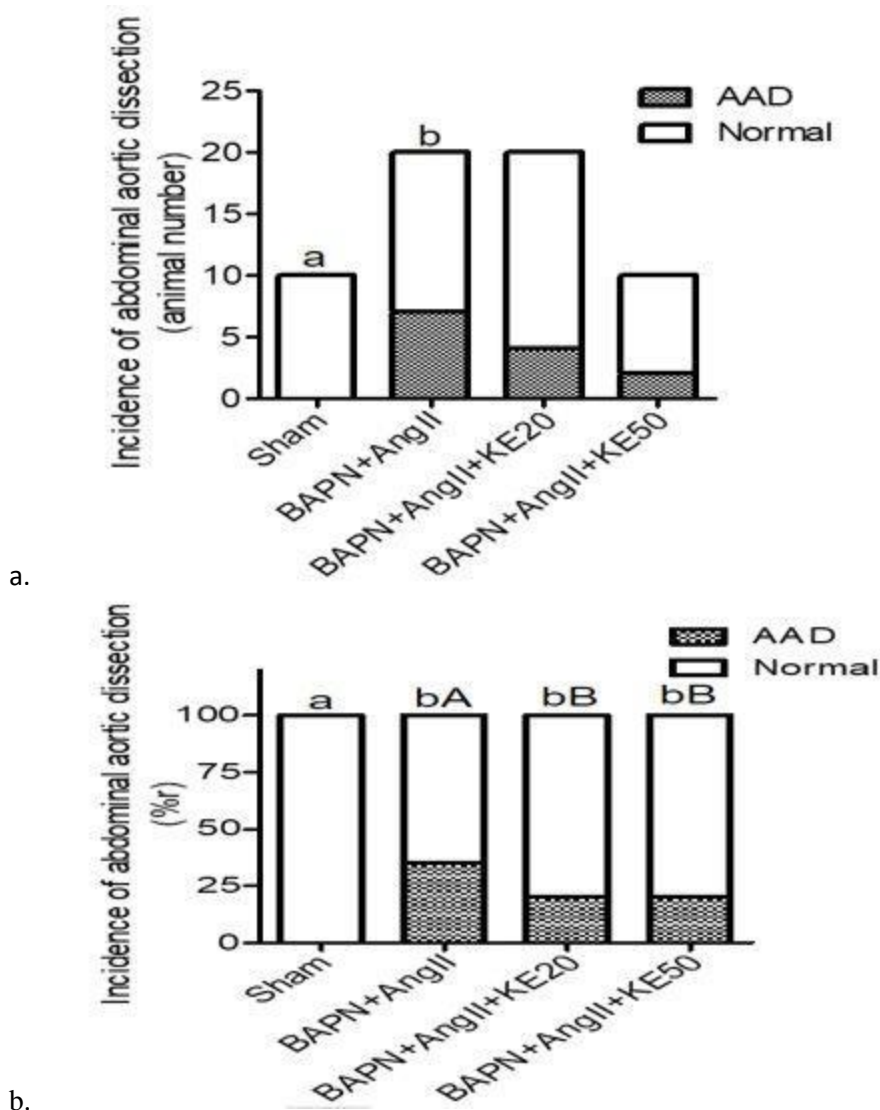


**Figure 5.** Survival rate of mice among the control group and model group. Survival rate (%) = total alive mice number by the end of the experiment (at 31 days)/total mice number in that group.





**Figure 6.** KE application reduces the incidence of TAD. 20KE and 50KE groups had no difference. a: Number of animals with TAD incidence. b: Percentage of TAD incidence. TAD: thoracic aortic dissection. a vs b, A vs B,  $P < 0.05$

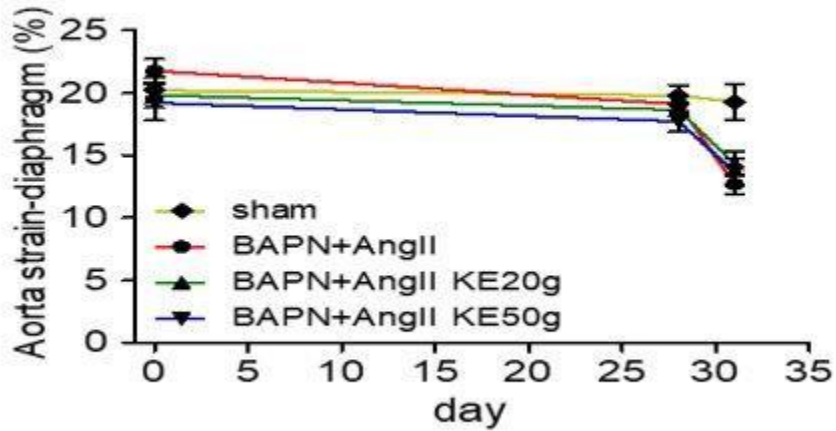


**Figure 7.** KE application reduces the incidence of AAD. 20KE and 50KE groups had no difference. a: Number of animals with AAD incidence. b: Percentage of AAD incidence. AAD: abdominal aortic dissection. a vs b, A vs B,  $P < 0.05$

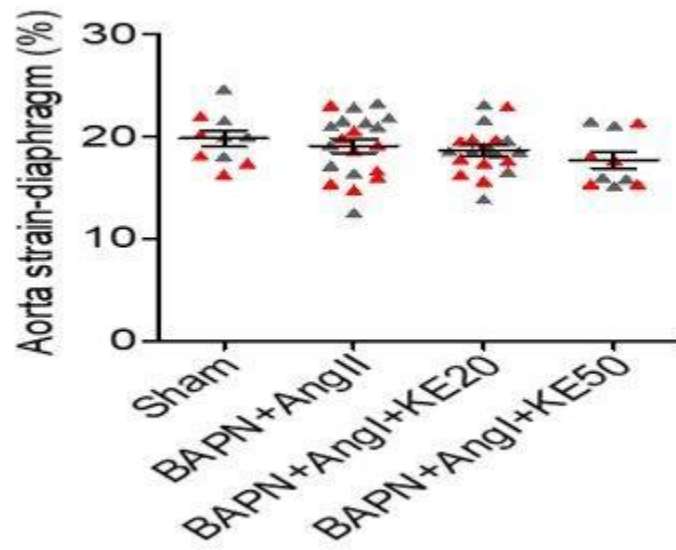
### 3.5 Ketone-ester Treatment does not Alleviate Aorta Stiffness

Since Ang II can increase aortic stiffness, we want to know whether ketone reverses the AngII-mediated aortic stiffness. We used ultrasound to measure the aorta strain at two locations: at the level of diaphragm (**Figure 8**) and the level of renal bifurcation (**Figure 9**). The aortic strain decreased in all BAPN+AngII, BAPN+AngII+KE20, and BAPN+AngII+KE50 groups. However, either BAPN or KE did not alter the aortic strain at the two tested locations (**Figure 8** and **Figure 9**). Male and female mice did not show

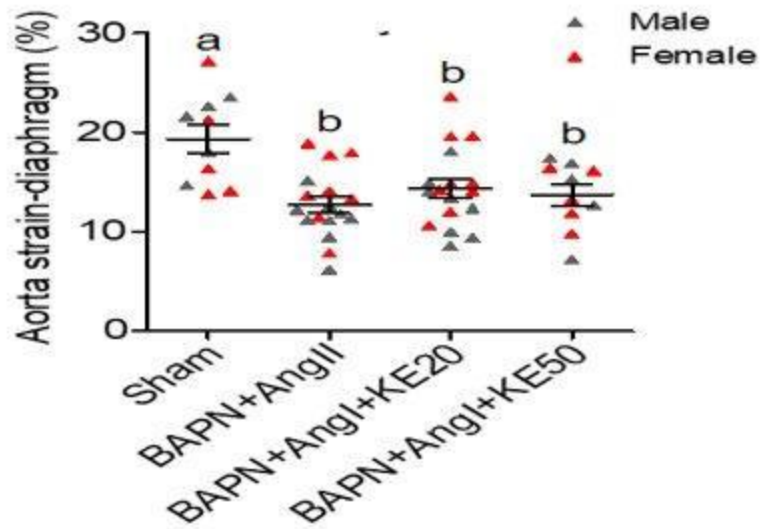
differences in arterial strain. These data suggest that KE treatment does not alleviate the aorta stiffness induced by Ang II.



a.

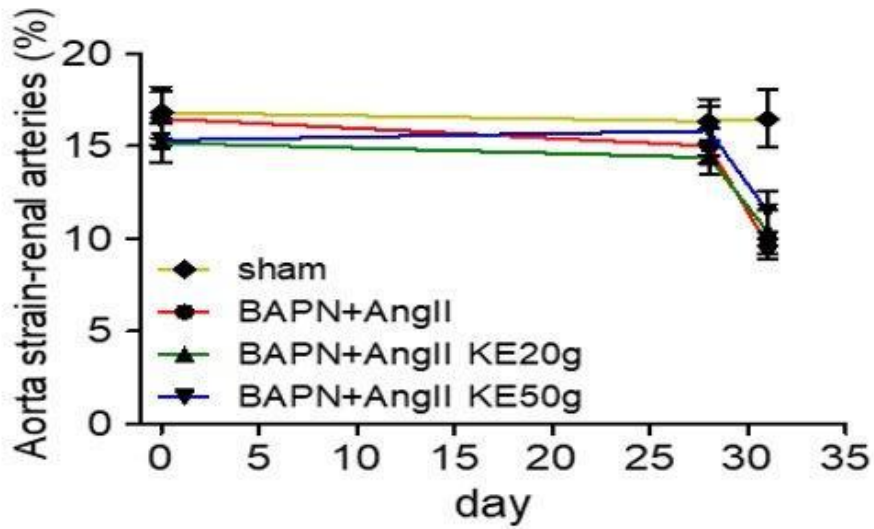


b.

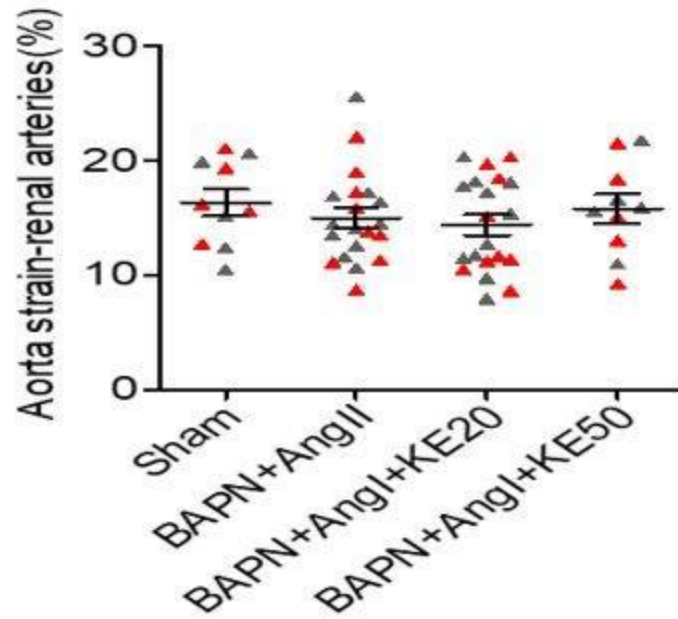


c.

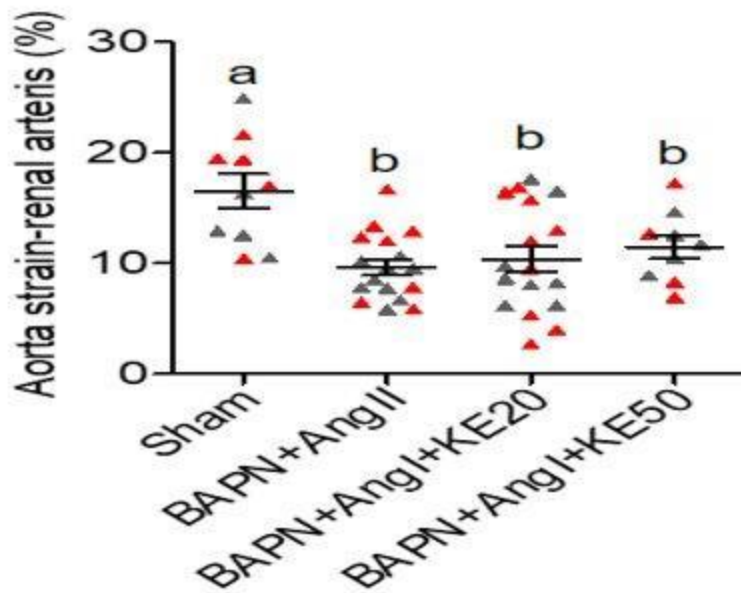
**Figure 8.** KE does not alleviate the vessel strain at the level of the diaphragm. a: Percentage of aortic strain at the level of the diaphragm. b: Percentage of aortic strain at the level of the diaphragm on day 28. c: Percentage of aortic strain at the level of the diaphragm on day 31. a vs b,  $P < 0.05$



a.



b.



c.

**Figure 9.** KE does not alleviate the vessel strain at the level of the renal bifurcation. a: Percentage of aortic strain at the level of the renal bifurcation. b: Percentage of aortic strain at the level of the renal bifurcation on day 28. c: Percentage of aortic strain at the level of the renal bifurcation on day 31. a vs b,  $P < 0.05$

#### 4. DISCUSSION

This study shows that ketone ester application reduces the incidence of TAD and AAD in mice. The mice were grouped into four groups; Sham (control), BAPN+Ang II,

BAPN+Ang II+KE 20g/L, and BAPN+Ang II+KE 50g/L. A higher dose of ketone ester was avoided because it could lead to reduced water consumption, animal dehydration, and cause death of the animals. Blood ketone levels were measured at three time points (11:00am, 4:00pm, and 11:00pm). Ketone levels measured during daytime (11:00am and 4:00pm) did not increase significantly which might be due to low mice activity during the daytime. Ketone levels measured during nighttime (11:00pm) are increased, more likely due to the regular mice active period. The measurement was done at age 8 weeks (about 2 months) before the Angiotensin II pump were implanted. The study shows that the use of low dose Ketone ester (20 g/L) did not improve survival rate compared to the BAPN+Ang II group. However, the use of medium dose (50 g/L) improves survival rate. The survival rate is determined by the total number of alive mice number by the end of the experiment (at 31 days) divided by the number of mice in that group. Thoracic aortic dissections and abdominal aortic dissections incidences were reduced with the application of ketone ester. The vascular strain (arterial flexibility) reduced after the application of angiotensin II. The stiffness of the vascular was not alleviated with ketone ester. Male and female mice did not show a difference in arterial strain. The body weight had no significant difference among mice groups, but Angiotensin II pump implantation slightly reduced their body weight. There was a reduction in water consumption after the application of BAPN and it was restored partially with ketone ester application.

This study has few limitations. It is not doubtful that animal models are valuable for biomedical research, but whether animal models are predictive for humans is disputable. There is no current effective aortic aneurysm drug therapy. The only effective treatment is surgical intervention (open surgical or endovascular stent placement). Anti-

inflammatory drugs, protease inhibitors, stem cell therapies, anti-platelet, anticoagulant drugs, and renin angiotensin system inhibitors may reduce the diameter of reestablished aortic aneurysm in mouse models and reduce the risk of aortic rupture in mice. (12)

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## VITAE

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### **EDUCATION/QUALIFICATIONS:**

#### **2021- till date: Georgia State University, Atlanta Georgia, USA.**

- Master of Interdisciplinary Studies with Biomedical Science and Enterprise Concentration

#### **2018-2020: Western Kentucky University, Bowling Green Kentucky, USA.**

- Master of Health Administration

#### **2005-2011: University of Ilorin, Ilorin Kwara, Nigeria.**

- Bachelor of Medicine and Surgery (MBBS)
- Core rotations in Internal Medicine, Obstetrics, and Gynecology, Pediatrics, Surgery, Radiology, psychiatry
- Active participation in rural (Community-Based Experience and Services) postings and community-based research works.
- Graduated among the top 10 from medical school.

#### **1998-2004: Ilorin Comprehensive High School, Ilorin Kwara, Nigeria.**

- West African Senior Secondary School Certificate (WASSCE)

### **CERTIFICATES:**

- ACLS Certified, 08/14/2023
- PALS Certified, 06/25/2024
- BLS Certified, 06/25/2024
- Enterprise Design Thinking Practitioner 2022
- Introduction to the Principles and Practice of Clinical Research 2021-2022
- Educational Commission for Foreign Medical Graduates 2021
- Live Saving Skill-Essential Obstetrics Care and Newborn Care: Liverpool School of Tropical Medicine/Royal College of Obstetrics and gynecologists 2017
- International Society of Ultrasound in Obstetrics and gynecology 2017

### **EXPERIENCE / EMPLOYMENT:**

#### **Volunteer Experience**

06/2020 - 08/2021: Respite Care Provider, Wendell Foster, Owensboro, KY, United States of America

- Provided the client assistance, companionship, and comfort
- Regular evaluation of the client's physical, mental, and emotional conditions.

- Administered prescribed medications and monitored vital signs.
- Facilitated appropriate professional intervention when required.

02/2019 - 05/2019: Volunteer Member, Tobacco-Free Campus, Western Kentucky University, Bowling green, KY, United States of America

- Oversaw the completion of various assessments and data collection activities to assess the campus community, environment, and climate.
- We educated students about tobacco and its health impact.
- Researched and collected data on current campus tobacco statistics
- Promoted cessation resources and services.

12/2018 - 05/2019: Member, Research and Planning Committee, Refugee Health Summit, Western Kentucky University, Bowling green, KY, United States of America

- As a research assistant at the Department of Public Health, Western Kentucky University, I was critical to the successful execution of the first-ever Western Kentucky University Refugee Health Summit.
- The summit was organized by the Department of Public Health in partnership with the International Center of Kentucky.
- My team and I ensured that the participants (mostly healthcare providers) were able to
- Understand the unique aspects of the provision of healthcare to refugees.
- Describe disease processes and health challenges prevalent in refugee groups. Employ appropriate strategies for implementing culturally and linguistically appropriate medical care to refugees.
- Identify and implement reduced-cost methods for improving language services for refugees.
- Build a network of stakeholders who are willing to join forces to impact public policy and improve refugee health.

04/2013 - 07/2013: Medical Officer, Internally Displaced People (IDP) Center, Kaduna, Nigeria

- The center was created for the Boko Haram insurgency victims (adults, children, and pregnant women).
- My team and I provided emotional and psychological support to those presenting with various psychiatric disorders like depression, anxiety, and PTSD.
- We provided medical services like blood pressure checks, blood glucose checks, and others.
- We referred the complicated cases that required expert attention to various tertiary centers.

03/2013 - 11/2016: Medical Officer, Rotary Club of Kaduna, Kaduna, Nigeria

- I participated in educating people on how to promote good mental health and prevent mental health problems.
- We supported existing local mental health groups, raised awareness via Health Fairs poster campaigns, and offered mentoring support in local schools.
- We supported people living with mental health issues and reduced stigma.

- We provided free primary healthcare services to underserved regions in Kaduna state.

01/2012 - 02/2012: Volunteer Staff, Ahmadu Bello University, Zaria, Nigeria

- As an intern at the hospital, I Participated in a community development program in the rural villages in Zaria.
- I was involved in promoting mental health awareness.
- We educated people on the importance of regular exercise and regular medical check-ups.
- Obtained history from patients, took patient vitals and carried out physical examinations

04/2008 - 02/2011: Member, Academic Committee, College of Health Sciences, Ilorin, Nigeria

- As a student at the College of Health Sciences, University of Ilorin,
- I represented the college in the state and regional medical quiz competitions.

## **Work Experience**

01/2022 - Present: Clinical Extern, Southern Regional Medical center, Atlanta, GA, United States of America

- Attending psychiatric inpatient cases with Dr. Okah Justin Anyokwu
- Documentation of patient medical history, mental status examination, patient workup, and treatment.
- Discuss cases and rationale for the selected treatment option with the attending Education of patients and involving their caregivers in the diagnosis, treatment plan, and community resources Chart review and review of laboratory results with the attending.
- Cases seen included: Agitated, manic, psychotic, and suicidal patients, among others.

09/2021 - Present: Clinical Extern, Avant Interventional Psychiatry, Atlanta, GA, United States of America

- Hands-on clinical experience in the Outpatient Unit with Dr. Okah Justin Anyokwu
- Activities involve acquiring experience in:
- Documentation of patient psychiatry history, complete mental status examination, patient workup, and discussion about treatment options and follow-up
- Writing patient notes (progress, hospital course, and discharge summary) and uploading them into Quadra med EMR after review by the attending.
- Use of doxy to follow-up patient and new patient intake
- Participating in morning reports on patients with attending, nurses, psychologists, peer counselors, social workers, etc.

09/2020 - 12/2020: Clinical Extern, Graves Gilbert Clinic, Bowling green, KY, United States of America

- Acquired adequate experience in the outpatient clinic

- Took detailed neurologic history and performed complete neurologic examinations
- Discussed management of various neurologic cases, including stroke, headaches, epilepsy, Alzheimer's disease, and others, with the attending.
- Worked as a team with the ancillary staff

08/2020 - 08/2021: Clinical Observer, Maple Therapy Service, Bowling green, KY, United States of America

- Acquired psychotherapy experience while observing a licensed Behavior Specialist and licensed Psychologist.
- Participated as a member of a Behavior Support team for the support of persons with major depression, borderline personality disorder, bipolar disorder, reactive attachment disorder, and multiple comorbidities

01/2020 - 07/2020: Administrative Intern, American Red Cross, Bowling green, KY, United States of America

- Developed plans, policies, and processes for health and wellness services and programs.
- Ensured compliance with all regulatory laws and policies.
- Promoted and implemented professional development within the organization.
- Managed health programs and services.
- Ensured all patient documentation is completed with extraordinary accuracy.
- Planned, managed, and evaluated health services and programs.

09/2019 - 03/2020: Clinical Observer, TJ Samson Community Hospital, Glasgow, KY, United States of America

- Observed medical practices, procedures, and patient care
- Took patient history and discussed cases with the attending physician.
- Fully supervised while examining patients in an inpatient setting.

01/2019 - 08/2019: Teaching Assistant, Dept. Public Health, Western Kentucky University, Bowling green, KY, United States of America

- Taught International Healthcare (HCA 347), an undergraduate-level course
- Attended lectures given by the instructor whom I am assisting.
- Evaluated student final papers, quizzes, examinations, and other assessments
- Developed teaching materials such as syllabuses, answer keys, supplementary notes, and course websites.

05/2018 - 08/2018: Clinical Extern, Neuropsychiatric Care Center and TMC Clinic, Greensboro, NC, United States of America

- Clinical experience with Dr. Mojeed Akintayo in the outpatient setting Experience acquired:
- Documentation of patient medical history, mental status examination, patient workup, and discussion of treatment options and follow-up
- Participated in the diagnostic formulation and management of patients with various psychiatric presentations

01/2016 - 01/2018: Senior Medical Officer, Specialist Hospital Offa, Offa, Nigeria

- Worked as a primary care physician Management of medical, obstetric, surgical, psychiatry, and pediatric cases in emergent and non-emergent settings
- Stabilized and performed necessary interventions and continually managed the cases.
- Coordinated patient referral to tertiary healthcare facilities as needed

03/2014 - 11/2016: Medical Officer/Medical Director, Nigerian Police Medical Services, Kaduna, Nigeria

- Coordinated medical teams to achieve daily goals.
- Managed the facility's budget
- Worked with other medical staff in this under-served community health center in the general outpatient and in-patient units
- I reviewed, discharged, and followed up with patients and performed basic medical procedures.
- Managed various acute and chronic medical conditions such as hypertension, headaches, seizure disorder, diabetes, acute diarrhea, delirium tremens, alcohol, and other drug intoxication, and provided a referral to tertiary centers for complex cases.

03/2013 - 12/2016: Medical Officer, Garden City Specialist Hospital, Kaduna, Nigeria

- Worked as a primary care physician
- Attended to patients in the inpatient and outpatient clinic units
- Managed emergency medical, psychiatry, obstetric, pediatric, and surgical cases
- Coordinated patient referrals to secondary and tertiary healthcare facilities as needed.
- Performed minor procedures such as insertion of a urinary and intravenous catheter, intramuscular and subcutaneous injections, phlebotomy, lumbar puncture, suturing of cuts, and episiotomies

03/2012 - 02/2013: Medical Officer, Medical Center, Nigerian Defense Academy, Kaduna, Nigeria

- A military university hospital.
- Worked as a primary care physician
- Hand-on management of medical, obstetrics, surgical, and pediatric cases in emergent and non-emergent settings
- We managed various acute and chronic medical conditions such as hypertension, headaches, seizure disorder, diabetes, acute diarrhea, delirium tremens, alcohol, and other drug intoxication.
- Referred patient to secondary and tertiary healthcare facilities as needed.

11/2011 - 02/2012: Clinical Intern, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

- The clinical internship is a year-long and required for full certification as a general practice physician in Nigeria.
- Ahmadu Bello University Teaching Hospital is a 550 bedded hospital.

- I acquired basic clinical skills under the supervision of seasoned health professionals in a high patient-load tertiary healthcare set-up.
- I worked as the first doctor on call in the emergency and on the inpatient unit, rotated under the supervision of attending in internal medicine, surgery, pediatric, obstetric, and gynecology.
- Performed minor procedures, assisted in surgeries, and participated in scholarly activities.
- Organized and led weekly case presentations and teaching rounds for medical students and supervised them.
- Organized and participated in monthly departmental morbidity/mortality meetings, case presentations, and medical conferences organized by the hospital.

09/2011 - 11/2011: Clinical Observer, Garden City Specialist Hospital, Kaduna, Nigeria

- Observed medical practices, procedures, and patient care
- Took patient history and discussed cases with the attending physician.
- Fully supervised while examining patients.

06/2011 - 09/2011: Clinical Observer, Balogun Hospital and Maternity, Ilorin, Nigeria

- Shadowed an obstetrician during clinic chart reviews, floor rounds, and surgeries

### **Research Experience**

09/2022 - Present: Research Assistant, Center for Molecular and Translational Medicine, Atlanta, GA, United States of America

Research Advisor: Dr. Ping Song

- I work at the Center for Molecular and Translational Medicine, Georgia State University, Atlanta, Georgia.

Research Title: Humane ApoE2 Endows Stronger Contractility in Rat Cardiomyocytes Enhancing the Heart Functions.

- Activities Involved:
- Non-invasive echocardiography was performed on rats.
- Arterial strain analysis was performed on rats' abdominal aorta using ultrasound.
- Rats' heart weight was measured after euthanization.
- Isolation and culture of rats' cells
- Histology and microscopy of sliced rats' hearts
- Cardiomyocytes contractility and intracellular Ca<sup>2+</sup> signaling
- Western blot assays of protein from rats' hearts

Research Title: The Effect of Ketone on Beta-aminopropionitrile-induced Vascular Remodeling Activities Involve: Research in progress.

03/2022 - Present: Research Assistant, Larkin Community Hospital, South Miami, FL, United States of America

Research Advisor: Dr. David Leszkowitz

- At the Larkin Community Hospital Research team, I am currently involved in research projects related to addiction medicine.
- One of the projects is the association between smartphone addiction and binge eating.
- Involve in literature reviews
- Participate in the formulation of questionnaires or primary surveys for research.
- Coordinate the administration of the primary surveys by the research participants.
- Involve in data analysis and interpretation.

08/2018 - 08/2021: Research Assistant, Dept. of Public Health, Western Kentucky University, Bowling green, KY, United States of America

Research Advisor: Dr. Michelle Reece

- I was involved in some funded scientific research projects and was critical to the successful execution of the Western Kentucky University Refugee Health Summit in April 2019.
- The first project was a Provider Needs Assessment in Refugee Health Services.
- The second was an Evaluation of the Implementation of Culturally and Linguistically Appropriate Services in the Southeastern United States.
- Lastly, Cross-sectional Analysis of the Risk Factors for Multiple Hospitalizations Among Female Medicaid Beneficiaries.
- Activities involved:
  - Data collection and analysis.
  - Used statistical software (SPSS, SARS, and Excel) to analyze data.
  - Planned and coordinated focus group discussions.
  - Planned and coordinated coaching sessions for research participants
  - Participated in the informed consent process, ensuring that human subjects, their families, and other health care providers clearly understand what is expected of and from them while participating in the project.

07/2010 - 01/2011: Student Researcher, Dept. of Community Medicine, University of Ilorin, Nigeria

Research Advisor: Professor T. m. Akande

- The World Health Organization (WHO) supported a program in which questionnaires were used to collect data on health status, as well as knowledge, attitude, and practices of the Pakata people on refuse management and the health implications.
- The analyzed data and the results were presented to the state ministry of health.
- The final report was sent to the World Health Organization.

### **PUBLICATIONS:**

- Ibrahim A. D., Reece M., Mkanta W., Alamri A., Pope D., Tadakaluru A., Thakur N., & Khatoon R. (2022, Aug). Cross-Sectional Analysis of the Risk Factors for Multiple Hospitalizations among Female Medicaid Beneficiaries Pub Status: Submitted.

- Wu Y., Zhao F., Ibrahim A., Yu C., Carr S., & Song P. (2022, Sep). Humane ApoE2 endows stronger contractility in rat cardiomyocytes enhancing the heart function Pub Status: Submitted.

### Online Publication

- Ibrahim A. D., Reece M., Mkanta W., Alamri A., Pope D., Tadakaluru A., Thakur N., & Khatoon R. (2019, November 04). Personal hygiene and the implications to health service among refugees in the USA. <https://apha.confex.com/apha/2019/meetingapp.cgi/Paper/446472> Pub Status: Published.

### Poster Presentation

- Ibrahim A. D., Reece M., Mkanta W., (2022, October 13). Healthcare Providers Perspectives on Types of Acculturations and Substance Abuse Behavior Among Refugees [Poster presented]. The Mental Health Services Conference/Washington, DC, USA
- Ibrahim A. D., Reece M., Mkanta W., Alamri A., Pope D., Tadakaluru A., Thakur N., & Khatoon R. (2018, November 15). Mental Health and Healthcare Access among Refugees in the USA. [Poster presented]. Kentucky Rural Health Association 20th Annual Conference/Bowling Green, KY, USA.
- Ibrahim A. D., Reece M., Mkanta W., Alamri A., Pope D., Tadakaluru A., Thakur N., & Khatoon R. (2019, March 15). Health Impact of Medical Interpretation Services for Linguistic Minorities [Poster presented]. 2019 Student Research Conference, Western Kentucky University/Bowling green, KY, USA.
- Ibrahim A. D., Reece M., Mkanta W., Alamri A., Pope D., Tadakaluru A., Thakur N., & Khatoon R. (2019, March 15). Oral Health Concerns in Refugees and Perceived Barriers to Care [Poster presented]. 2019 Student Research Conference, Western Kentucky University/Bowling green, KY, USA.
- Ibrahim A. D., Reece M., Mkanta W., Alamri A., Pope D., Tadakaluru A., Thakur N., & Khatoon R. (2019, June 15). Policy Implications for Mental Health Service Utilization among Refugees in America. [Poster presented]. North American Refugee Health Conference, /Toronto, ON, CAN.

### Oral Presentation

- Ibrahim A. D. (2011, December 11). Water and electrolyte Balance [Oral Presentation]. Departmental Grand Round at Ahmadu Bello University Teaching Hospital/Zaria, NGA
- Ibrahim A. D. (2021, November 16). TNF-Alpha Gene Silencing Mediated by Orally Targeted Nanoparticles Combined with IL-22 for Synergistic Combination Therapy in Ulcerative Colitis [Oral Presentation]. Research Meeting, Institute of Biomedical Science, Georgia State University/Atlanta, GA, USA.
- Ibrahim A. D. (2022, February 22). Metformin Suppresses Diabetes Accelerated Atherosclerosis via the Inhibition of Drp-1 Mediated Mitochondrial Fission [Oral Presentation]. Research Meeting, Institute of Biomedical Science, Georgia State University/Atlanta, GA, USA.



- Ibrahim A. D. (2022, March 03). Brain-Derived Autophagosome Profiling and Engulfment of Nucleoid-Enriched Mitochondrial Fragment by Autophagy in Neurons [Oral Presentation]. Research Meeting, Institute of Biomedical Science, Georgia State University/Atlanta, GA, USA
- Ibrahim A. D. (2022, June 04). Effect of Topiramate on Acid-Base Balance [Oral Presentation]. Clinical Meeting in Avant Interventional Psychiatry/Atlanta, GA, USA.
- Ibrahim A. D. (2022, September 06). iPSC-Derived Human Microglia-like Cells to Study Neurological Diseases [Oral Presentation]. Research Meeting, Institute of Biomedical Science, Georgia State University/Atlanta, GA, USA.

### **Online Publication**

- Ibrahim A. D., Reece M., Mkanta W., Alamri A., Pope D., Tadakaluru A., Thakur N., & Khatoon R. (2019, November 04). Personal hygiene and the implications to health service among refugees in the USA. <https://apha.confex.com/apha/2019/meetingapp.cgi/Paper/446472> Pub Status: Published.

### **HOBBIES & INTEREST:**

- I enjoy traveling, especially taking road trips.
- I derive pleasure from spending time with my family and friends.
- I am innovative in nature, and trying new things gives me satisfaction and fulfillment.
- I love watching soccer and playing soccer.

### **OTHER AWARDS/ACCOMPLISHMENTS:**

- Enterprise Design Thinking Practitioner 2022
- Preventing and Managing Crisis Situation (PMCS) 2019
- Certified Opioid Overdose Prevention First Responder 2019
- Certified Mental Health First Aider 2019
- National Youth Service Corps of Nigeria (NYSC) Award of Recognition of National Service-2013
- Member, Western African College of Physicians (PRIMARY) - 2013
- Chief Intern – 2012

### **MEMBERSHIP AND HONORARY/PROFESSIONAL SOCIETIES:**

- Association of Nigerian Physicians in the Americas -2022
- American Medical Association - 2020
- American College of Healthcare Executives-2019
- American Public Health Association - 2019
- Nigerian Medical Association - 2011

- Medical and Dental Council of Nigeria -2011