UNIVERSITY of RWANDA

COLLEGE OF MEDICINE & HEALTH SCIENCES

SCHOOL OF MEDICINE & PHARMACY

DEPARTMENT OF SURGERY

A COMPARATIVE STUDY OF APPENDICITIS INFLAMMATORY RESPONSE SCORE AND ABDOMINAL ULTRASOUND IN EVALUATION OF PATIENTS WITH ACUTE APPENDICITIS AT UNIVERSITY TEACHING HOSPITAL OF KIGALI (CHUK).

Dissertation submitted in partial fulfillment of the requirements for the award of the Degree of Masters of Medicine in General Surgery of the University of Rwanda

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Kigali, May 2019

DECLARATION

Researcher:

I solemnly declare that this dissertation entitled **"A comparative study of appendicitis inflammatory response score and abdominal ultrasound in evaluation of patients with acute appendicitis"** is a bonafide and genuine research work carried out by me unless stated otherwise. It has not been submitted to any university in Rwanda for the award of any degree or professional qualification.

Signature _____ Date _____

Dr RWAGAHIRIMA Elisée

Supervisors:

I hereby declare that this dissertation has been submitted with my approval as the supervisor.

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ACKNOWLEDGEMENT

Any work I take up in life would be incomplete if I don't begin it with acknowledging Dr NIFASHA Antoine and Dr ABAHUJE Egide who were my guide in conducting this study. Your patience, motivation and immense knowledge you put into this thesis will always be appreciated. Thank you. The knowledge I've gained from you will make me a better Surgeon.

I would like to thank my biggest support system, my family. It is only because of them I stand today as a doctor, following my dreams to become a surgeon. Thank you.

My heartfelt gratitude goes to Prof John TARPLEY for being someone with a lot of experience in research and publication, he has been the one who taught me everything I know about research methodology. Thank you, Sir.

I would like to extend a warm gratitude to our respected academic head of surgical department, Dr NTIRENGANYA Faustin, for his unflinching encouragement and support throughout. My experience in surgery has been one of the best I could have asked for.

I would like to thank Dr NTAGANDA Edmond, Dr CURCI Michael, and Dr MPIRIMBANYI Christophe for your practical advice and guidance.

My thanks go out to The Chairman and all the members of the Institutional Ethical Committee, for approving our study and giving us valuable suggestions to improve it.

I take this opportunity to thank the whole teams of surgery department at CHUK.

I wish to thank my classmates, real friends who made my journey in residency enjoyable.

I am deeply grateful to thank Dr KAGIMBANGABO J.M.V for his indispensable help and advice concerning statistical analysis throughout this thesis.

Last, but most definitely not the least, I would like to thank patients. As always, their support and their belief is what makes any study successful.

Dr RWAGAHIRIMA Elisée

DEDICATION

This thesis is wholeheartedly dedicated in loving memory of my father MPANGAZA Festo who gave me the thirst for new knowledge and the potential to seek it. You will always be my inspiration.

My warmest thanks to my dearest mother NYIRAKANYANA Anastasie, for her love, encouragement and belief in me. She continually provides moral support and emotional support.

I would like to give a big warm hug to my siblings: ABAHUJINKINDI Colette, late SEMANA, MUSONI James, KAYUMBA Théodore, MUKAKAYANGE Violette, NIYONSHUTI Claudine, NIYONSABA Claudine, MWIZA Claudette, UMWALI Odette, NEZA Wilbert, and MPANGAZA Jean Claude for your love and support. I have spent many happy moments with you.

To my role models Prof Ahmed KISWEZI and Dr LULE Joseph

Lastly, to the Almighty God who gives the power of mind, strength and protection.

I dedicate this work.

LIST OF ABBREVIATIONS

AIR score: Appendicitis Inflammatory Response Score

AUC: Area under the curve

CHUK: Centre Hospitalier Universitaire de Kigali

CI: Confidence Interval

CRP: C - reactive protein

CT: Computed tomography

DH: District Hospital

HC: Health Center

Lab: Laboratory

LMICs: Low-and Middle-Income Countries

M: F: Male-to-Female ratio

NPV: Negative predictive Value

PPV: Positive predictive value

OR: Operating Room

ROC: Receiver Operating Characteristic curves

RWF: Rwandan francs

RIF: Right iliac fossa

SPSS: Statistical Package for the Social Sciences

U/S: Ultrasound

WBC: White Blood Cell

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ABSTRACT

Background: Acute appendicitis is a common disease in surgical practice. Its usual presentation is often not classical, leaving a diagnostic problem in some cases. Using a scoring system that incorporates the inflammatory variables such as AIR score can improve and overcome this drawback.

Aim of the study: To compare AIR score and abdominal U/S in evaluation of patients with acute appendicitis and to determine if AIR score can decrease the time and cost of care of patients with acute appendicitis.

Patients and Methods: This prospective descriptive observational study included 42 patients who underwent appendectomy from June 2018 to May 2019. All parameters included in the AIR score and U/S results were collected and statistical analysis performed using SPSS version 21.0. Descriptive statistics and diagnostic performance of AIR score and U/S were compared.

Results: We found 26 males and 16 females, M: F was 1.62:1. Age range was 7-55 years. Peak age: 26-35 years, with a mean of 31.26 years. The mean symptoms duration was 2.4 days. AIR score ranged from 5 to 12. 26 patients were classified into the indeterminate group and 16 patients into high-probability group. U/S request was associated with a longer mean time from admission to surgery (11 hours versus 5.3 hours). AIR score had a sensitivity and specificity of 43% and 100% respectively, while U/S had sensitivity and specificity of 92% and 20% respectively. AIR score demonstrated a higher specificity (100%) in high probability group while U/S showed a better sensitivity and specificity for indeterminate group of 94% and 100% respectively. U/S had a higher PPV (100%) than AIR score (86%) and AIR score showed a better NPV (67%) compared to U/S (19%). The ROC area of AIR score was 0.738 for AIR score and 0.562 for U/S ($p = 0.09$). Negative appendectomy rate was 11.9%.

Conclusion: AIR score is more specific and accurate in high probability patients and also convincingly select patients who need abdominal U/S for diagnosis. Abdominal U/S is better at confirming the diagnosis or to rule out the possibility of appendicitis in equivocal cases.

Keywords: Acute appendicitis, AIR score, U/S.

I. INTRODUCTION

Acute appendicitis is an acute inflammation of the appendix, occurring mainly following obstruction of its lumen.

Worldwide, acute appendicitis is the most common indication for emergency surgery, its incidence is estimated at 1.17 per 1000 and lifetime risk of 8.6% in men and 6.7% in women[1]. It is associated with high morbidity and occasional mortality related to failure of making an early diagnosis[2]. There are classical signs and symptoms of acute appendicitis, nevertheless, in many patients initial features are atypical or nonspecific as other gastrointestinal tract disease can mimic acute appendicitis[2,3] .

In the management of acute appendicitis, early diagnosis and prompt surgical intervention is the key for successful management. Perforation and peritonitis are due to delayed misdiagnosis. Appendicitis inflammatory score is among various scoring systems developed to aid in the diagnosis of acute appendicitis[4].

I.1 BACKGROUND

Diagnosing acute appendicitis still remains a common surgical problem. Accurate diagnosis can be aided by additional testing or expectant management or both[5]. Moreover, the complicated forms of appendicitis such as appendicular perforation are sometimes results of in hospital delays to diagnosis. In 2011, Aly Saber et al found that delay in diagnosis of acute appendicitis is associated with a more advanced stage of disease and a higher morbidity. Delayed diagnosis can be minimized by careful attention to a thorough patient's history, physical examination and early clinical consult. Appendicitis with a delay in treatment usually leads to high perforation rates, and unfavorable outcome[6].

A study conducted in 2005 in the Netherlands found the negative appendectomy rate of 15% of the patient; a number similar to another large Swedish study[4]. Another study done in the North America reported the negative appendectomy rate of 13%.

It is safe to assume that the negative appendectomy rate declined to approximately 10% with the routine use of U/S[7]. The higher sensitivity of computed tomography (CT) seems to have had an even greater effect on the negative appendectomy rate, which has decreased even further to 5–10%[7,3] . In`

many european countries, most surgeons still consider acute appendicitis to be a clinical diagnosis and do not routinely perform imaging studies[8].

Scoring systems have been developed to help in clinical assessment of patients with acute appendicitis. Alvarado score construction was based on a review of patients who had been operated with suspicion of appendicitis, whereas the Appendicitis Inflammatory Response (AIR) score is supposed to be used on all patients with suspicion of appendicitis. Many studies have shown the importance of C-reactive protein (CRP) in the assessment of acute appendicitis and it is not incorporated in Alvarado score[3,8]. The recently introduced AIR score was designed to overcome these drawbacks[8].

U/S is probably more widely available in Africa and is the first abdominal imaging routinely used in diagnosis of appendicitis at university teaching hospital of Kigali, Rwanda. It has sensitivity rates of 55-96% and specificity rates of 85-98% while CT scanning achieves sensitivity rates of 92-97% and specificity rates of 85-94%. Despite the relatively high degree of accuracy of these imaging tests, their role in daily management is unclear. Cases with high clinical scores can be readily managed surgically without further imaging. Similarly those with low scores can be excluded. Imaging is probably best reserved for those cases in which clinical diagnosis is indefinite[9]. AIR score would work as a tool that hasten and increases the accuracy of decision-making and at the same time reduces the need of harmful and expensive imaging. We aim at comparing AIR score and abdominal U/S in diagnosing acute appendicitis for patients who present in national referral hospital of low and middle income countries.

I.2.PROBLEM STATEMENT

This study was designed after realizing that many patients with acute appendicitis have to pass through an array of investigations being biological or radiological. Preliminary data showed that 94% of all patients had abdominal U/S done before surgical management. This negatively impacts patients in terms of money and time required to access definitive care. The time required for a patient with acute appendicitis to get surgical care is not yet known. But retrospective records outlined an average time of 16 hours from admission to surgery.

I.3. JUSTIFICATION OF THE STUDY

This study will show the accuracy of AIR score in diagnosis of acute appendicitis and its contribution to decreasing the waiting time and cost of care in patients with acute appendicitis.

The results of this study may help to use the tool not only to predict the outcome but also to improve the quality and safety of management provided to patients with appendicitis managed in referral hospitals of Rwanda.

I.4. RESEARCH QUESTION

Can AIR score decrease the time and cost of care required for management of acute appendicitis?

I.5. OBJECTIVES

1.5. 1.General objective

To determine if AIR score can decrease the time and cost of care of patients with acute appendicitis

1.5.2. Specific objectives

- Determine the proportion of patients with suspected acute appendicitis who undergo diagnostic U/S.
- Determine the duration between diagnostic U/S request and results for patients with acute appendicitis.
- Determine the duration required to get AIR score for patients with acute appendicitis.
- Assess the diagnostic accuracy of AIR score and U/S in acute appendicitis.

II. LITERATURE REVIEW

The natural history of acute appendicitis is similar to that involving other hollow visceral organ. The sequence of events starts with inflammation of the wall followed by ischemia, perforation with subsequent the development of abscess or generalized peritonitis[4,10]. Obstruction is frequently implicated but not always required for the development of acute appendicitis. In non perforated appendicitis, increased intraluminal pressure is present in only one third of the patients[3].

Obstruction may result from a variety of causes including: Fecalith, calculi, lymphoid hyperplasia, infectious processes, parasites and benign or malignant tumors. Once obstruction occurs, continuous mucus secretion leads to an increase in luminal and intramural pressure and acts as closed loop obstruction resulting in thrombosis and occlusion of vessels and edema. Resident bacteria start to proliferate.

Visceral afferent nerve fibers are stimulated by engorgement, leading to vague central or periumbilical abdominal pain as well as reflex anorexia, nausea and vomiting. Classical right lower quadrant pain ensues when inflammatory process involves the serosa of the appendix, hence the adjacent parietal peritoneum[4].As the condition progress, the wall of the appendix becomes ischemic and then necrotic. Bacteria leak out through the wall followed by pus formation within and around the appendix. Aerobic organisms predominate early in the course, while mixed bacteria are more common in late stage.

The time course longer than 48 hours is associated with high perforation rate. Jones RP et al reported that 20% of patients developed perforation less than 24 hours after the onset of symptoms. 65% of patients in whom the appendix perforated had symptoms for longer than 48 hours[10].

It is still challenging to make early and correct diagnosis so that unnecessary appendectomies and complications are reduced. This may be due to the non specificity of initial symptoms that may confuse treating physicians resulting in delayed of surgical decision-making.

Atypical presentation (children, elderly, pregnancy) results in delayed diagnosis of appendicitis especially patients without typical complaints of right lower quadrant pain and those lacking a proper physical examination, or those received analgesia[10].

Appendicitis inflammatory response score was developed in 2008 in Sweden based on prospectively collected data of variables with independent prognostic value using a mathematically more appropriate method for the construction[11].

The AIR score is made of clinical and laboratory variables including vomiting, pain in the right lower quadrant, body temperature, high white blood cell count, proportion of polymorphonuclear leukocytes, and a high level of C-reactive protein[4].

Table 1: Appendicitis inflammatory response (AIR) score

Diagnostic variables	**Score**
Vomiting	1
Pain in right lower quadrant	1
Rebound tenderness or muscle defense	
▪ Light	1
▪ Medium	2
▪ Strong	3
Body temperature>38.5	1
Polymorphonuclear leukocytes	
70-84%	1
≥85%	2
White blood cell count	
10-14.9x10^9/L	1
≥15x10^9/L	2
C-reactive protein concentration	
10-49g/L	1
≥50g/L	2
Total score	**12**

Interpretation:

Sum 0–4: **Low possibility**: Discharge and follow up.

Sum 5–8: **Indeterminate group**: In-hospital active observation with rescoring/imaging or diagnostic laparoscopy

Sum 9–12: **High probability**: Surgical exploration.

Previous studies have shown AIR score has a high discriminating power and outperforms Alvarado score ($p<0.05$)[3]. It avoids unneeded admissions and investigations in patients in whom the diagnosis is indefinite.

In developed countries, imaging has been the first modality to diagnose acute appendicitis; and increases progressively in LMICs hospitals especially sub Saharan Africa. Despite the progress, clinical diagnosis remains the gold standard and imaging has got variable specificity and sensitivity. Moreover, clinical exam and scoring systems have the highest power in diagnosing acute appendicitis, reducing negative appendectomies, and avoid unnecessary admissions[12]. Osman et al. 2010 have found that the accuracy of the clinical diagnosis of acute appendicitis was 80%, while that of the CT scan and U/S were 78% and 44%, respectively[13].

In other similar studies, U/S was inconclusive in 44% of cases and provided an accurate diagnosis in only 28% of patients[12]. On other hand, CT scan has higher accuracy than U/S in diagnosing acute appendicitis but its scarcity is remarkable in most of hospitals of LMICs and where available, its cost and accessibility is limited. Sensitivity and specificity is up to 97 % and 94% respectively, even in non-contrast CT scan, it is still around 93% sensitivity and 96% specificity[14].

As noted in different series, clinical diagnosis could probably be more accurate in our settings compared to imaging.

III. METHODOLOGY

III.1. Study design

This was a prospective descriptive observational study including all patients with acute appendicitis admitted at CHUK from June 2018 to May 2019.

III.2. Geographical area

This study was conducted in the department of surgery at University Teaching Hospital of Kigali (CHUK), a public and main referral hospital in the country located in the centre of Kigali city which receives around 70% of all transfers to tertiary care level. It has got 565 beds and 6 operating theater and the department of surgery accounts for 170 beds shared among 8 surgical subspecialties.

III.3. Study population

Our study included all patients admitted at Accident and Emergency departments (both adult and pediatric) with right iliac fossa pain and who were suspected for acute appendicitis.

III.4. Selection of study population

III.4.1.Inclusion criteria

- All patients presenting to CHUK adult and pediatric emergency departments with right iliac fossa (RIF) pain, with suspicious of acute appendicitis.

III.4.2.Exclusion criteria

- Patients with post traumatic right iliac fossa pain

III.5. Sampling methods

All patients meeting the selection criteria, during the study period, were included in the study after offering an assent or informed consent.

III.5.1. Sample size calculation

No current available database on prevalence of acute appendicitis in Rwanda. Sample size required was calculated at **http://epitools.ausvet.com.au/** to estimate a proportion or apparent prevalence with specified precision with the help of previous data from Ministry of Health Annual statistics in 2010 where 95 patients with acute appendicitis were reported and operated. Also the study done by Babatunde et al in Nigeria the incidence of acute appendicitis was 0.05%[15].

Following input values were used at **http://epitools.ausvet.com.au/**

Confidence level = **0.95**, Estimated true proportion = **0.05**, Desired precision = **0.05**, Population size (for finite populations) =**95 patients**

Therefore, we needed a sample size of **42** patients.

III.6. Variables

Demographic characteristics included age, gender, referral province, district hospital referral, District Hospital length of stay, and insurance status. Data from disease process included: Elapsed time from the onset of symptoms to arrival at hospitals, symptoms, vital signs, physical examination and laboratory findings, time from clinical suspicion to investigations, U/S results, time to OR ,findings in OR, cost of imaging and laboratory investigations.

III.7. Enrollment, data collection

Patient were enrolled after being examined by a physician and suspected to have acute appendicitis as first differential. Every patient entered in the study after offering in informed consent. Upon admission, patients were asked about clinical symptoms and their duration. Demographic data were recorded. AIR score was calculated after necessary clinical and laboratory investigations are obtained. Duration from examination and investigations to availability of results was recorded. Decision to request U/S or not belongs to the treating doctor. Patients were followed up till operation theatre. Intra-operative findings were recorded for all patients.

III.8. Data management

Data were collected using a pre tested data collection form during recruitment and follow up of data were then be entered in excel database and analyzed using SPSS 21.0. The analysis was based on frequency distribution, charts and figures; cross tabulation as well as well as specificity, sensitivity, predictive values of both AIR score and U/S were calculated. The diagnostic accuracy of AIR score versus U/S was calculated based on intra-operative findings. We used t-test and Chi-square test to compare the variables, and p-value< 0.05 was considered to be statistically significant.

III.9. Ethical considerations

III.9.1.Confidentiality

During patients' recruitment and follow up, there was no change about the process of care of enrolled patients. The information was kept confidential by the research team. No any patient's identification was mentioned on the data collection forms. A separate paper with patient identification number was used to help in patient follow up and was destroyed after data validation before analysis

III.9.2.Informed consent

An informed consent was obtained from the patient or any other legally recognized attendant at the recruitment. Patients had the right to refuse study enrollment. Patients were informed that their decision had no any impact on treatment decisions or medical management.

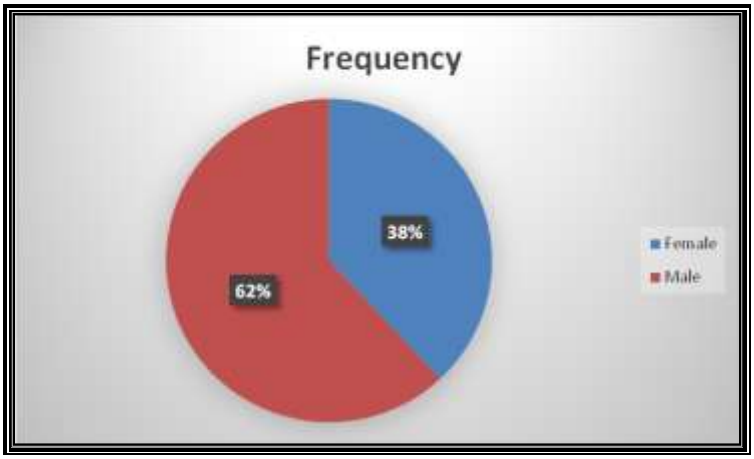
III.9.3.Ethical approval

The research proposal was submitted and presented to the Department of Surgery for approval, then to Institutional Review Board of College of Medicine and Health Sciences (CMHS-IRB). The research proposal was also approved by ethic and research committee of University Teaching Hospital of Kigali (CHUK).

IV.RESULTS

During the study period, a total of 42 patients underwent appendectomies. Statistical analysis was performed with AIR score and abdominal U/S.

Figure 1: Gender distribution



Out of 42 patients, 26 (62%) were males while 16 (38%) patients were females.

Male to female ratio 1.62:1

Table 2: **Age-wise distribution of patients**

Variable	Frequency N (%)
Age(years)	
</=15	6(14.3)
16-25	6(14.3)
26-35	15(35.7)
36-45	11(26.2)
>/=46	4(9.5)

Patients' age ranged from 7 to 55 years old with mean age of 31.26 years. Peak age incidence was high (35.7%) in the third decade followed by age group of 36-45 years and 9.5 % of patients above the age group of 45 years were affected.

Table 3: Signs and symptoms distribution

Variable	Frequency N (%) Yes
Anorexia	27(64.3)
Nausea	36(85.7)
Vomiting	34(81)
RIF pain	42(100)
Rebound tenderness	36(88.1)

All patients presented with right iliac fossa (RIF) pain (100%) followed by vomiting (81%). Rebound tenderness was observed in 36 out of 42 patients (88.1%).

Table 4: Symptoms duration and vital signs distribution

Variable	Mean	95%CI	Median	95% CI
Symptom duration	2.4 days	2.1-2.7	3	2-3
Systolic Blood Pressure (mmHg)	118	114-123	116	112-123
Diastolic Blood Pressure (mmHg)	72	69-75	70	69-75
Heart rate (beats per minute)	94	89-99	95	86-101
Temperature(˚C)	37.3	37-38	37	36.8-37.5
SaO_2 (%)	96	94-97	97	95-98

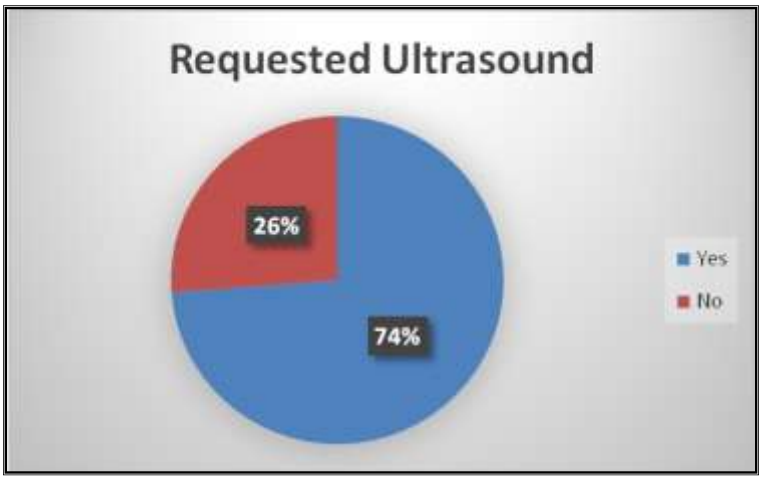
The elapsed time from the onset of symptoms to arrival at hospitals in appendicitis patients was 2.4 days (57h36mins).The mean temperature was 37.3˚C (range 36 ˚C to 40 ˚C).

Table 5: Laboratory findings distribution

Variable	Frequency N (%)
WBC	
<10	16(38.1)
>10	26(61.9)
Neutrophils	
<70	12(28.6)
>70	30(71.4)
CRP	
<40	27(64.3)
>40	15(35.7)

WBC elevation was observed in 26 (61.9%) patients along with increase in neutrophil polymorphs in 30 (71.4%) patients in present study

Figure 2: U/S request distribution



Diagnostic abdominal U/S was requested in 74% (31/42) of patients

Table 6: U/S request according to AIR score probability

AIR score group	No U/S request N (%)	U/S requested N (%)	Chi-square	p-value
Indeterminate (5-8)	7(26.9)	19(73.1)	0.041	0.891
High probability (9-12)	4(25)	12(75)		

In this study, minimum AIR score recorded was (5) and the maximum was (12). No statistical difference in U/S request depending on AIR scores probability. 75% of U/S were requested among patients with high probability AIR score while 73.1% of U/S request with regard to group of indeterminate probability AIR score.

Table 7: Mean time between investigation and intervention

Variable	Mean (hours)	95% CI
Time from U/S to result	6.8	4.7-9.1
Time from lab request to result	1.53	1.23-1.84
Time from admission to surgery	12	9.5-14.5
Result to Surgery	4.6	3.8-5.5

The mean time to get U/S results was 6.8 hours and the mean time to get laboratory results was 1.53 hours.

Table 8: Comparison of time from admission to surgery for AIR score and U/S (t-test)

Variable	U/S requested in hours	No U/S requested in hours	P value
Mean time from admission to surgery	11	5.3	**<0.001***
Mean time from result to surgery	4.6	2.9	**0.032***
Mean time from lab to result	1.5	1.2	0.272

There is the statistically difference between mean time from admission to surgery comparing patients with U/S request to those without U/S request ($p<0.001$), mean time: 11 hours versus 5.3 hours. The same applies from results to surgery ($p=0.032$), mean time: 4.6 hours versus 2.9 hours. No statistical difference between mean time from lab investigations request to results for clients with U/S request to those without U/S request.

Table 9: Comparison of mean time from lab investigations request to results to the mean time from U/S request to results. Paired-samples t-test

Variables	Mean (hours)	Standard deviation	P-value
Time from lab request to result	1.53	0.903	**<0.001**
Time from U/S request to result	6.80	6.335	

The mean time to get lab results (1.53 hours) was significantly different to the mean time to get U/S results (6.80 hours) with p value< 0.001.

Table 10: Correlation of AIR score probability according to diagnosis

AIR score	No appendicitis N (%)	Appendicitis N (%)	Chi-square	p-value
Indeterminate probability (5-8)	5(19.2)	21(80.8)	3.493	0.062
High probability (9-12)	0(0)	16(100)		

Out of 42 patients operated for appendicitis, 88% (37/42) of patients were found with appendicitis. No negative appendectomy (0%) observed in high probability group. In indeterminate patients (no definite appendicitis), only 19.2% (5/26) of patients were found to have the normal appendices while 21 patients (80.8%) were found to have acute appendicitis at operation, which would result in a higher false negative rate.

No statistical difference found in diagnosing appendicitis among people with indeterminate and high probability (p-value=0.839). Diagnosis of appendicitis was 100% in high probability group and 80.8% in indeterminate probability group.

Table 11: Correlation of U/S with intra-operative findings

U/S	Intra-operative findings		
	Normal	Appendicitis	
Positive	4	24	(90.3%)
Negative	1	2	(9.7%)
Total	5 (16.1%)	26(83.9%)	

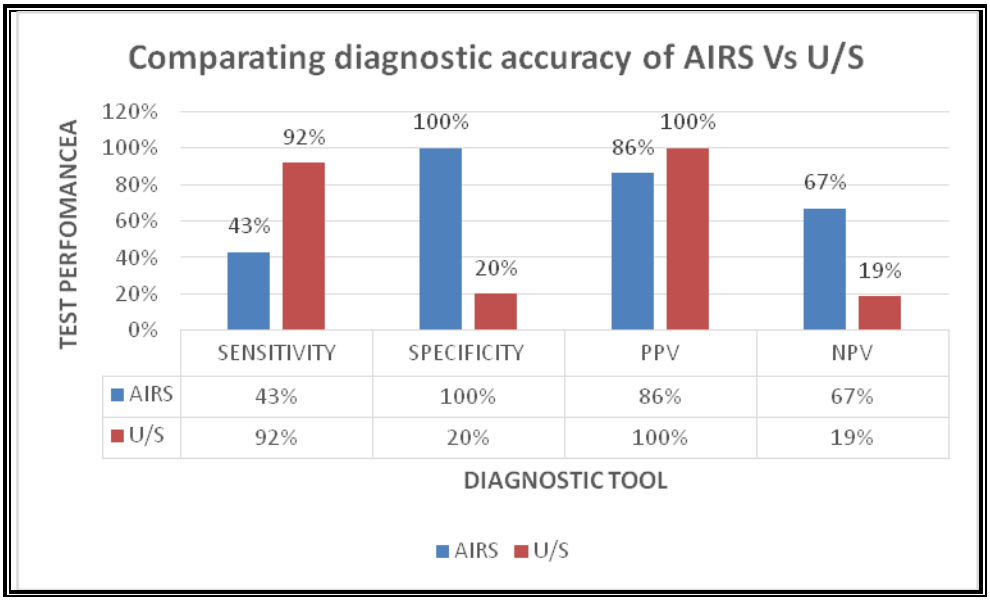
Abdominal U/S examination had been performed in 31 patients (74%). It established a diagnosis of appendicitis in 28 patients (90.3%) while in 3 patients (9.7%) the appendix was described normal or not visualised. Diseased appendices were found in 83.9% of operated patients and normal appendices were 16.1%. Out of 26 patients who actually had appendicitis, 24(true positive) were positive on U/S. False positivity and negativity of U/S were 4/24(14.3%) and 2/3(66.7%) respectively.

Table 12: U/S sensitivity and specificity according to the AIR score

Score	Specificity (%)	Sensitivity (%)
5-8	100	94
9-12	0 (4 false negatives and 0 true negatives)	89

U/S was associated with high specificity (100%) and sensitivity (94%) in indeterminate probability group.

Figure 3: Comparison of diagnostic accuracy of AIR score and U/S



The proportion of patients who got U/S request and found to truly have the disease was 92% (sensitivity) while sensitivity for AIR score was 43%, this means that U/S performs better when it is requested as confirmatory exam. With regard to specificity, the AIR score has a much higher specificity of 100% than U/S (20%); this means that AIR score can be a good appendicitis diagnostic tool to rule in appendicitis.

The probability of patient to have appendicitis when a test is positive known as positive predictive value was 100% for U/S and 86% for AIR score. With regard to negative predictive value defined as probability of missing appendicitis when the test is negative was 67% for AIR score while it was 19% for U/S.

Figure 4: Receiver operating characteristic (ROC) curve to compare the performance of U/S versus AIR score

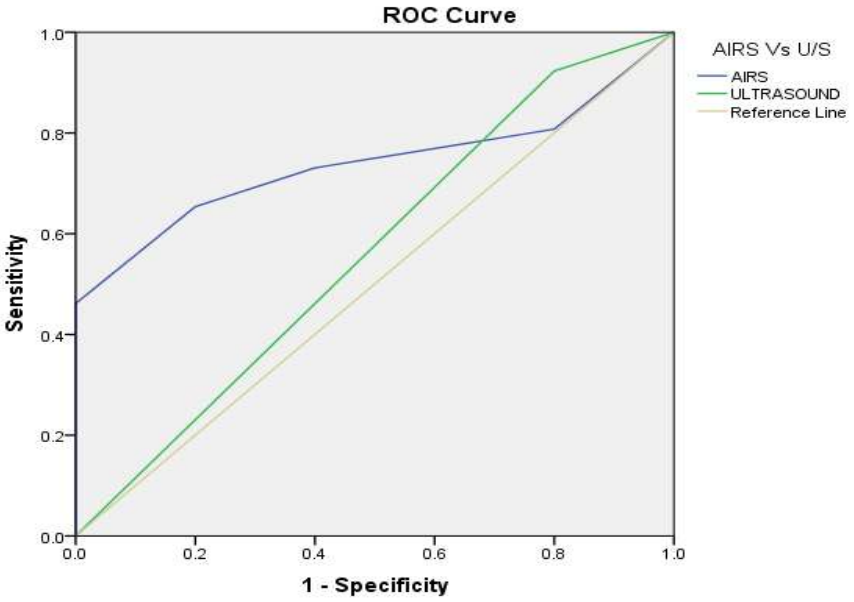


Table 13: Statistical significance of area under the curves (AUC)

Variable	Area	95% CI	P-Value
AIR score	0.738	0.562-0.915	0.090
U/S	0.562	0.267-0.856	0.150

Generally, AIR score performed better than U/S in diagnosing appendicitis with the area under the curve of 0.738 although it was not statistically significant (p value: 0.09).

Cost of care: Full blood count was asked for all patients studied. Considering the cost of abdominal U/S at CHUK of 10250 RWF compared to CRP cost of 8000 RWF which resulted in cost increment of 2250 RWF.

V. DISCUSSION

This study assessed if the use of AIR score in diagnosing appendicitis can decrease the time from admission to the time of surgery in a referral hospital from a Low and Middle Income Country. We also compared the accuracy of abdominal U/S versus AIR score in diagnosing or ruling out appendicitis.

In the present study the number of male patients (62%) is more than female patients (38%) with a male to female ratio of 1.62:1.These findings are similar to what was reported by Subash K C et al[16] . In the study conducted by Hale et al 64% of patients were males and 36% were females[6,17]. These findings are consistent with our study. Appendicitis is considered as a disease of young population. In our study, the age was ranging from 7 to 55 years and maximum number belonged to third decade of life (26-35 years: 35.7%). The mean age was 31.26 years comparable to the mean age of 31.26 years reported by Nina-Astrid Nde Ouedraogo et al in their study on diagnosis of Acute Appendicitis in Sub-Saharan Africa[18].Mean duration of symptoms was 2.4 days (57h36min) which is consistent with the findings of Bruno VON-MÜHLEN et al[19]. In contrast to our findings, Richard Nshuti reported the mean duration of symptoms of 4.5 days[2]. Also, Christophe Mpirimbanyi et al, in 2017 reported 4 days duration of symptoms before presentation to the health system due to delays in patients seeking care, reaching care and in receiving care[20].

This difference can be explained by the fact that the Rwandan health system is improved, the referral system is good and the majority of Rwandans are covered by Community Health Insurance. There are provincial hospitals and people don't have to travel long distance to have surgery[21].

All patients (100%) presented with right iliac fossa pain. Vomiting was the second most common symptom seen in 81% of total patients. And rebound tenderness was observed in 36 out of 42 patients (88.1%). The clinical features are not different from other studies. Dr. Sudershan Kapoor et al found predominance of pain (90%) followed by vomiting (82%) which correlates well to our findings[22]. This differs from a study done by Mohamed Kamel El-Mezayen et al in Egypt, 2018 where anorexia was the second symptom in 86% of patients[23].

Total white cell account was raised in 26 (61.9%) cases along with neutrophilia in 30 (71.4%) cases in present study. These results were comparable to the study done by Subash K C et al[16].Findings from Nshuti R. et al showed that WBC is not reliable in diagnosis of acute appendicitis due to its low sensitivity and NPV[2].

In this study we found that 31 (74%) patients with suspected appendicitis underwent U/S and the diagnosis was confirmed in 28 (90.3%) patients. In 3(9.7%) patients, the appendix was normal.

Nina-Astrid Nde Ouedraogo studied the diagnosis of Acute Appendicitis in Sub-Saharan Africa and found results similar to our findings, where abdominal U/S had been performed in (72.1%) and diagnosis of appendicitis was made in (86.2%)[18]. Sheraz R. Markar in his study: A comparative international study on the management of acute appendicitis between a developed country (United Kingdom) and a middle income country (Sri Lanka) stated that U/S was used more commonly in the Sri Lanka group when compared to the United Kingdom group (64.5% versus 31.5%; P < 0.001) and advocated for U/S as the first imaging modality. Also suggested that selective use of CT scan where U/S has failed to provide a diagnosis[24].

The negative appendectomy rate in our study was 12%. These findings are comparable with the findings of Narendra JB et al, who reported negative appendectomy rate of 12%[25]. Jaffar Alkhuzaie et al in their study"Could Preoperative U/S Examination Improve the Final Outcome of Appendectomies?" 12.3% of patients had negative appendectomy[12]. S. T. Edino reported (Nigeria), the overall negative appendectomy rate of 14.1% comparable to our findings. Early appendectomy is advocated by many surgeons to avoid perforation, accepting a negative appendectomy rate of about 15-20%[26].

Our study results showed that U/S request was associated with delay to get surgery. There is statistical difference between mean time from admission to surgery comparing patients who got U/S to those who didn't get U/S request (mean time 11 hours versus 5.3 hours) (p<0.001).

In relation to this, the time from results to surgery (p=0.032), mean time of 4.6 hours (U/S requested) versus 2.9 hours (no U/S requested) this may be due to the fact that people who had U/S requested might take much time to get result and to confirm the diagnosis. There was no statistical difference between mean time from lab investigations request to results for patients with U/S request (1.5hours) to those without U/S request (1.2 hours) (p = 0.272).

The mean time to get lab investigations results (1.53 hours) was significantly different to time to get U/S results (6.8hours) (p value< 0.001).The delays can be explained by few radiologists, radiologists not available in the hospital especially during night, weekend and holidays.

As observed by Col Jyotindu Debnath et al in the study on imaging in acute appendicitis, in many countries the use of U/S is limited by lack of available radiologists whenever needed or off working hours[27]. U/S should be requested selectively especially in equivocal cases to prevent complications when the diagnosis is made at a late stage.

Chang Sik Shin et al in 2014 came up with comparable results the average time form admission to incision of 9.6 hours. The average time from admission to diagnosis was 3.0 hours. The average time from diagnosis as appendicitis to surgery was 6.6 hours[28].

In this study, all 42 patients were classified as indeterminate-to-high probability of acute appendicitis (AIR score: 5 to 12). Overall, AIR score had higher specificity (100%) i.e. could rule out appendicitis better than U/S. The U/S had higher sensitivity (92%) than AIR score i.e. ability to identify appendicitis correctly.

The AIR score classified 16 (38%) patients to the high-risk group with a specificity of 100%. All of them had appendicitis. They could undergo immediate surgery without any negative appendectomies thus safely preventing additional and costly confirmatory imaging. As observed by Aijaz Ahmad Malyar et al in India, high specificity of AIR score makes it a supportive tool in decision making and identifying patients that should benefit from immediate surgery[29]. No literature found to report low specificity for AIR score.

Similar results were also reported by A. J. Scott et al where high-risk cut-off demonstrated excellent specificity (97%) for appendicitis[30]. A score of greater than 8 points had a lower sensitivity for AIR score in diagnosing acute appendicitis compared with U/S.

No definite diagnosis of appendicitis was made in remaining 26 (62%) patients (indeterminate group). 5 (19.2%) of them were found to have the normal appendices while 21 (80.8%) were found to have acute appendicitis at operation, which would result in a higher false negative rate. AIR score was unable to exclude appendicitis in those deemed indeterminate probability.

U/S was associated with excellent specificity (100%) and sensitivity (94%) in patients grouped as indeterminate. In this instance, U/S study confirmed the diagnosis of appendicitis in patients where the clinical presentation was doubtful.

Comparable results were reported by Seung-Hum Yu et al in his meta-analysis on evaluation of U/S in the diagnosis of appendicitis that showed 98% for the sensitivity and specificity with a conclusion that U/S is more useful for those patients who have an indeterminate probability of acute appendicitis after the initial evaluation[31]. Sheraz R. Markar et al also advocated for the use of U/S as a first-line imaging in the assessment of patients with clinically equivocal signs[24].

The positive predictive value of U/S (100%) was found to be higher than that of AIR score (86%). Probability of appendicitis in positive U/S is more than in a positive AIR score. But probability of patient being negative appendectomy is more in negative AIR score (NPV: 67%) than negative U/S (NPV: 19%). Narendra JB also reported a high PPV (95.12%) of U/S[25]. Manne Andersson who constructed AIR score in 2008 reported a comparable NPV (76%) of AIR score in high risk patients[4].

Comparing AIR score and U/S using ROC curve analysis, AIR score had better value of AUC than that of U/S, indicating improved performance of AIR score to correctly classify patients suspected for appendicitis. This is consistent with the findings of Henna E Sammalkorpi et al[1].

Full blood count was asked for all patients studied. However, considering the cost of abdominal U/S at CHUK of 10250 RWF compared to CRP cost of 8000 RWF which resulted in cost increment of 2250 RWF. It was difficult to estimate the total cost of management of acute appendicitis with the use of AIR score or U/S due to intra-operative details that are individualized according to patient's condition, duration of procedure and materials used.

U/S is non-invasive and doesn't require special preparation; but its routine request may lead to extra expenditure, a financial burden for patients coupled with delayed surgical intervention.

Out of 31 abdominal U/Ss requested, 12 (39%) of them were ordered in patients grouped as high probability. This would have caused a 39% reduction in U/S scanning. Therefore, additional U/S costs can be saved as long as U/S will not add any benefits in high probability patients. It would be reserved for diagnostic precision in indeterminate patients. Nina-Astrid Nde Ouedraogo et al reported comparable findings in 2018[18].

Study limitations

- Improper documentation and accuracy of the history taking and the interpretation of physical signs. This would result in incorrect AIR score calculation.
- Self-medication using analgesic, antipyretic or antibiotic at the onset of symptoms can generate a bias for the calculation of the AIR score. We were unable to control it.
- U/S accuracy remains highly operator dependent.

VI. CONCLUSION AND RECOMMENDATIONS

VI.1.Conclusion

This study concludes that, AIR score may be appropriate for selecting patients who require immediate surgery or further evaluation with abdominal U/S. It remarkably decreases waiting time to surgery. During operation, all patients who scored with an AIR score compatible with high probability had appendicitis. It significantly reduces the number of negative appendectomies. Our findings showed that patients in indeterminate category would benefit the maximum from abdominal U/S which resulted in improved diagnostic accuracy along with the AIR score.

In LMICs, use of AIR score could be a good alternative to U/S especially for high probability group to help decide who can be operated straight away without any extra imaging. It would avoid not only unnecessary cost, but also delays in management, delays which can lead to complicated appendicitis.

AIR score may be used as an adjunct to surgical decision-making. It may be of great importance particularly in restricted working hours, as it facilitates clinicians, at emergency department, a quick assessment and decision making for patients with suspected appendicitis by its simplicity to use and to apply.

Diagnostic abdominal U/S will continue to play a large role in the evaluation of patients with suspected appendicitis who have an indeterminate AIR score.

VI.2.Recommendations

- To CHUK, AIR score should be approved and its implementation can reduce the need for unnecessary diagnostic imaging in patients with suspected appendicitis.
- To CHUK Accident and Emergency and surgical department, abdominal U/S should be ordered selectively when diagnosis is in doubt (indeterminate score).
- Adherence to AIR score will increase diagnostic accuracy, leading to timely intervention, and largely eliminating the costs of unnecessary imaging or observation.

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APPENDIX I: QUESTIONNAIRE

DEMOGRAPHICS

Study ID:

Age (years):

Gender: Male Female

Province of origin: EASTERN WESTERN NORTHERN SOUTHERN KIGALI CITY

Referring hospital/private clinic

Profession: Student farmer employed unemployed

Insurance: Mutuelle None Other: If YES specify…….

Telephone number

DISEASE CHARACTERISTICS

Duration of symptoms (days)

Passed at health center before consulting district hospital: YES or NO.

If YES, Time spent at HC in days……

Time of arrival at DH……..

Time spent at DH in hours……..

Investigations done at District Hospital: FBC: **Yes/No** CRP: **Yes/No** U/S: **Yes/No**

Management at DH: Antibiotics: **Yes/No** Perfusions: **Yes/No** Analgesics: **Yes/No** Surgery: **Yes/No**

Date of referral to CHUK…….

Mode of transport: Ambulance private public

PATIENT'S COURSE AT CHUK

Date of admission

Time of admission

Admission Vital signs: BP …… HR ……. Temperature …. RR … Oxygen saturation….

Past medical history: Diabetes Mellitus: YES/NO……. Hypertension: YES/NO…….

Past surgical history: YES /NO If YES specify

Signs and symptoms: Anorexia…….. Nausea……. Vomiting…….

Right iliac fossa (RIF) pain ….. RIF tenderness

Temperature….. Other…..

Investigations: LABS: FBC (WBC…..Hemoglobin……Neutrophils…….), CRP…… (g/l) and U/S result

Time of lab request…..

Time of imaging request……

Time of imaging results (hours)……

Time for lab results…….

Time of operation……..

Operator: Resident Consultant

Intra-operative findings: Normal Inflamed Gangrenous Perforated

Other.....

APPENDIX II: CONSENT AND ASSENT FORMS IN ENGLISH AND KINYARWANDA

CONSENT FORM IN ENGLISH

TITLE OF THE STUDY: A comparative study of appendicitis inflammatory response score and abdominal U/S in evaluation of patients with acute appendicitis at CHUK.

I, …… agree to participate in the study
"A comparative study of appendicitis inflammatory response score and abdominal U/S in evaluation of patients with acute appendicitis at CHUK".

I am aware that participation in the study is voluntary and I will not be paid for the participation. In addition, all information provided will be treated with confidentiality and that my anonymity will be maintained.
I am aware that the result of this study may be published but I will not be identified as an individual. I reserve the right to withdraw from the study at any time if I so wish.

…….. …… …….
Name of participant Signature of participant Date

……. …….. …….
Name of researcher Signature of researcher Date

Principle researcher contacts: Dr RWAGAHIRIMA Elisée
E-mail: eligain@gmail.com, Tel: 0788884353

Chairperson Institutional Review Board CMHS Prof Kato J. NJUNWA Tel 0788490522

CONSENT FORM IN KINYARWANDA

AMASEZERANO YO KWEMERA KUJYA MU BUSHAKASHATSI

UBUSHAKASHATSI:" A comparative study of appendicitis inflammatory response score and abdominal U/S in evaluation of patients with acute appendicitis at CHUK

Jyewe, …….. nemeye kujya mu ubushakashatsi bwitwa "**A comparative study of appendicitis inflammatory response score and abdominal U/S in evaluation of patients with acute appendicitis at CHUK**" Nasobanuriwe ko kujya muri ubu bushakashatsi ari ubushake bwanjye, ko ntagihembo ntegereje guhabwa, kandi ko nzagirirwa ibanga kugiti cyanjye ndetse n'amakuru yose nzatanga.

Nasobanuriwe ko ibizava muri ubu bushakashatsi bizatangazwa ariko ko ntazerekanwa nk'umuntu ku giti cye.

Mfite uburenganzira bwo kuva muri ubu bushakashatsi igihe cyose nabishakira.

…… …….. …….
Amazina n'umukono by'uwasobanuriwe Italiki

…… …….. …….
Amazinay'umushakashatsi Umukonow'umushakashatsi Italiki

Ukeneye ibindi bisobanuro wahamagara:

- Uyoboye ubushakashatsi: Dr RWAGAHIRIMA Elisée
    - E-mail: eligain@gmail.com
    - Nimero za telefoni: 0788884353

- Abajyanama:
    -
    -
    -
    - Chairperson Institutional Review Board CMHS:
      Prof Kato J. NJUNWA Tel 0788490522

ASSENT FORM (for children)

Project title: "**A Comparative study of appendicitis inflammatory response score and abdominal U/S in evaluation of patients with acute appendicitis**.

Investigator: Dr RWAGAHIRIMA Elisée Tel: **0788 884353** Email: **eligain@gmail.com**

We are doing a research study aiming at comparing **appendicitis inflammatory response score and abdominal U/S in evaluation of patients with acute appendicitis.** If you decide that you want to be part of this study, you will be asked by a clinician to answer questions related to the study.

You can ask questions any time, now or later. You can talk to the doctors, your family or someone else. You do not have to be in this study, no one will be mad at you if you don't want to do this. We will also ask your parents or guardians if they would like you to be in the study. Even if you say yes now, you can change your mind later.

When we are finished with this study, we will write a report about what was learnt. This report will not include your name or that you were in the study.

ASSENT

I want to take part in this study. I know I can change my mind at any time, without any consequence to the health care provided to me.

Name of the child:

……..

Name and signature of the next of kin

……

Verbal assent given: Yes **Date**: … /… /……

I confirm that I have explained the study to the participant to the extent compatible with the participant understands, and that the participant has agreed to be in the study.

Name of person obtaining the assent and signature:

…….. ……**Date**: … /… /……

ICYEMEZO CYUBURENGANZIRA BWO KWINJIRA MUBUSHAKASHATSI (ABANA)

UMUTWE W'IBYIGWA: "A **comparative study of appendicitis inflammatory response score and abdominal U/S in evaluation of patients with acute appendicitis at CHUK.** Umushakashatsi: Dr RWAGAHIRIMA Elisée Telefoni: 0788 884353.

Turakora ubushakashatsi kuri "**A comparative study of appendicitis inflammatory response score and abdominal U/S in evaluation of patients with acute appendicitis at CHUK, Rwanda.** Niwemera kwitabira ubu bushakashatsi, umuganga azagira ibibazo akubaza bijanye no kuvura ububabare ku barwayi bagize ubushye.

Ushobora kubaza abaganga cyangwa umuryango wawe, cyangwa undi muntu uwo ariwe wese.

Ushobora kubaza ikibazo igihe icyo ari cyo cyose. Ntabwo ari itegeko kwitabira ubu bushakashatsi. Ntawe uzakurakarira nuba utabyitabiriye.Tuzabaza n'ababyeyi bawe niba bemera ko witabira ubu bushakashatsi. Nubwo wakwemera ubu wemerewe kuva muri ubu bushakashatsi igihe cyose ushakiye kandi nta ngaruka byagira ku buvuzi uhabwa.

Niturangiza ubu bushakashatsi,tuzandika amakuru y'ibyo twabonye ariko izina ryawe ntaho rizagaragara.

Nemeye kwitabira ubu bushakashatsi

Izina ry'umwana……..

Izina ry'uhagarariye umwana

……

Itariki…….

Izina ry'uhagarariye umwana

……

Ndemezako nsobanuriye uwitabiriye ubu bushakashatsi kurwego abisobanukirwa bituma yemera kwitabira.

Amazina y'usobanuriye uwitabiriye……..

Itariki…….

Mu gihe hakenewe ibisobanuro izi nomero zishobora kwifashishwa

- Uyoboye ubushakashatsi: Dr RWAGAHIRIMA Elisée
    - E-mail: eligain@gmail.com

- Nimero za telefoni: 0788884353

- Abajyanama: Dr NIFASHA Antoine Telefoni: 0782018377

  Dr ABAHUJE Egide Telefoni: 0788660562

- Abajyanama:

  - Chairperson Institutional Review Board CMHS:

    Prof Kato J. NJUNWA Tel 0788490522

APPENDIX III: ETHICAL APPROVAL

UNIVERSITY OF RWANDA **COLLEGE OF MEDICINE AND HEALTH SCIENCES**

Office the Academic Head, Department of Surgery, School of Medicine and Pharmacy

Kigali, April 04th, 2018

To the CMHS IRB Committee:

I am writing in support of Dr Elisée RWAGAHIRIMA's application for IRB Approval to conduct a Research entitled: **A comparative study of appendicitis inflammatory response score and abdominal ultrasound in evaluation of patients with acute appendicitis at CHUK.**

Dr Elisée RWAGAHIRIMA is a third year (PGY III) student in the General surgery MMed program in the Department of Surgery. The proposed research aims at comparing appendicitis inflammatory response score and abdominal ultrasound in evaluation of patients with acute appendicitis at CHUK.

This is aproposal for dissertation to be submitted in partial fulfillment of the requirements for the award of the degree of Master of Medicine In General Surgery of the University of Rwanda.

Dr RWAGAHIRIMA has presented his research study to the faculty in the department of surgery and has obtained the departmental clearance to carry on this study. He was assigned Dr NIFASHA Antoine as supervisor and Dr Egide ABAHUJE as co-supervisor.

If he obtains the CMHS IRB approval the Department of surgery will continue to support his efforts to contribute to the management of surgical patients.
If any clarification is needed, please feel free to contact me at 0788732667 or at fostino21@yahoo.fr

Very respectfully,

Dr NTIRENGANYA Faustin
CHIRURGIEN

Dr. NTIRENGANYA Faustin, MD,MMed, MCS, DiU, DUCC
Senior Lecturer
Academic Head of the Department of Surgery

UNIVERSITY OF RWANDA **COLLEGE OF MEDICINE AND HEALTH SCIENCES**

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 23rd /07/2018

Dr RWAGAHIRIMA Elisée
School of Medicine and Pharmacy, CMHS, UR

Approval Notice: No 266 /CMHS IRB/2018

Your Project Title ***"A Comparative Study Of Appendicitis Inflammatory Response Score And Abdominal Ultrasound In Evaluation Of Patients With Acute Appendicitis At University Teaching Hospital Of Kigali(CHUK)"*** has been evaluated by CMHS Institutional Review Board.

		Involved in the decision		
			No (Reason)	
Name of Members	**Institute**	Yes	**Absent**	**Withdrawn from the proceeding**
Prof Kato J. Njunwa	UR-CMHS		X	
Prof Jean Bosco Gahutu	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS	X		
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Landrine	Kicukiro district		X	
Dr Gishoma Darius	UR-CMHS	X		
Dr Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umutesi Jeannine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 24th May 2018, **Approval has been granted to your study.**

Please note that approval of the protocol and consent form is valid for **12 months**.

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol or consent form must be submitted to the committee for review and approval, prior to activation of the changes.
2. Only approved consent forms are to be used in the enrolment of participants.
3. All consent forms signed by subjects should be retained on file. The IRB may conduct audits of all study records, and consent documentation may be part of such audits.
4. A continuing review application must be submitted to the IRB in a timely fashion and before expiry of this approval
5. Failure to submit a continuing review application will result in termination of the study
6. Notify the IRB committee once the study is finished

Sincerely,

Date of Approval: The 23rd July 2018

Expiration date: The 23rd July 2019

for Professor Kato J. NJUNWA
Chairperson Institutional Review Board,
College of Medicine and Health Sciences, UR

Cc:
- Principal College of Medicine and Health Sciences, UR
- University Director of Research and Postgraduate Studies, UR

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

August 6th, 2018 **Ref.: EC/CHUK/628/2018**

Review Approval Notice

Dear Elisée Rwagahirima,

Your research project: ***"A comparative study of appendicitis inflammatory response score and abdominal ultrasound in evaluation of patients with acute appendicitis at CHUK"***

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 6th August 2018 to evaluate your protocol of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your protocol.

You are required to present the results of your study to CHUK Ethics Committee before publication.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

ETHICS COMMITTEE CHUK

Dr. Rusingiza Emmanuel
The President, Ethics Committee

University Teaching Hospital of Kigali<<***University teaching hospital of Kigali Ethics committee operates according to standard operating procedures (Sops) which are updated on an annual basis and in compliance with GCP and Ethics guidelines and regulations***>>

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