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INFORMATION

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MOLECULAR CHARACTERIZATION OF PLASMODIUM FALCIPARUM KELCH-13 AMONG FEBRILE PATIENTS IN SELECTED GOVERNMENT HOSPITALS IN NIGERIA

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ABSTRACT:

Malaria is a life-threatening disease caused by protozoan *Plasmodium* species. *Plasmodium falciparum* is the deadliest species. Reducing and eliminating malaria burden are linked to most of the Sustainable Development Goals (SDG), central to SDG3 targeting the end of malaria by 2030. This study was aimed at assessing the Management of malaria and prevalence of *P. falciparum kelch-13* among febrile patients in selected Government Hospitals in Nigeria. Malaria patients (399) attending outpatient clinics of the Hospitals between August, 2019 and January, 2021, were enlisted in the study, following ethical approval and informed consents. Blood (5mL) was collected from patients for microscopic and molecular investigation of malaria parasite. DNA extraction, PCR amplification, BLAST, and alignment were performed. *Plasmodium* resistance to Artemether/lumefantrine was determined by PCR amplification of extracted DNA using *Kelch-13* gene primer. Data obtained were subjected to One-way Analysis of Variance and Linear Regression. The VapA gene primer amplified 55 (68.75%) out of the 80 DNA extracts tested. Twenty-five strains of *P. falciparum* belonging to 3 clades phylogenetically were identified and they showed evolutionary relationships with others. *Plasmodium falciparum* resistant *Kelch-13* gene was detected in 70% of the isolates. This study observed a high prevalence of resistant gene to ACT drugs in the study area. Monitoring the effectiveness of ACTs must be done routinely to ensure timely changes in National treatment policies.

Keywords: *Febrile, Hospitals, kelch-13, Malaria, Molecular, Plasmodium falciparum, Resistant.*

INTRODUCTION:

Plasmodium falciparum is a malaria-causing protozoan parasite and it's one of the several species of *Plasmodium.* Infected female Anopheles mosquitoes, known as malaria vectors, transmit malaria parasites by biting their prey at night and in the early morning hours [1]. The parasite is classified into Kingdom - Protista, Phylum - Apicomplexa, Class - Aconoidasida, Order - Haemosporida, Family - Plasmodiidae, *Genus - Plasmodium and Species - falciparum* [2].

Almost 94% of all global malaria cases were reported in the WHO's African Region in 2019, which is estimated at 215 million cases. The consistent efforts and increased awareness of malaria control and prevention measures have resulted in a 29% reduction in malaria mortality rates worldwide between year 2000 and 2019 [3]. Malaria continues to be a major problem in Sub-Saharan Africa. Nearly all malaria deaths occurred in the sub-Saharan region, where 90% of cases and 92% of deaths occurred in 2015 [3]. There are certain groups of people who are more susceptible to malaria infection; immune-compromised individuals, such as those with HIV/AIDS, pregnant women, infants under the age of five, and immigrants are all included in this category. Most of the world's cases were concentrated in 29 countries, with Nigeria accounting for 27% of the total [3].

In spite of the fact that there were 204 million fewer malaria cases reported in the WHO African Region in 2000 than there were in 2019, the incidence of malaria decreased from 363 to 225 cases per 1000 population at risk during this time period, highlighting the difficulty in interpreting changing disease transmission in a rapidly growing population in the region [3]. The population of the WHO African Region grew from 665 million in 2000 to 1.1 billion in 2019. More than seventy-eight percent of this region's cases of malaria have decreased from about 18 cases per 1000 people at risk in 2000 to about four cases today [3]. From around 25 deaths per 100,000 people at risk in 2000 to 12 in 2015 and 10 in 2019, the global malaria fatality rate has been steadily declining [3]. As a whole, only 31 countries were responsible for 95% of the global malaria deaths [3].

Malaria deaths in 2019 were estimated to be 43% in Nigeria (23%), followed by the DRC (11%), Tanzania (5%) and Mozambique (4%). This year, Nigeria had the highest number of global malaria cases (27%), and deaths (23%), [3]. 33 million pregnancies were estimated in the WHO African Region in 2019, of which 36% (12 million) were malaria-infected during pregnancy [4]. East and Southern Africa had the lowest prevalence of malaria exposure during pregnancy (24%).

A key element in malaria prevention and treatment is the availability of effective antimalarial medications. Resistance to Artemisinin-based combination therapies, for example, puts at risk the global effort to lessen malaria's impact. As of now, all malaria-endemic countries recommend Artemisinin combination therapy (ACT), with Artesunate (injectable) as the main treatment for severe malaria.

There is a link between the prevalence of *Pf-Kelch13* genetic variations and Artemisinin resistance [5].

As PCR is far more accurate than microscopy and can detect 5 parasites/L of blood with 100% accuracy and equal specificity, it's the most important research technology at the moment [5]. For studying strain variation, mutations, and parasite genes involved in treatment resistance, PCR techniques are extremely useful [5]. Rapid real-time PCR (Real-time PCR, Quantitative Nucleic Acid Sequence Based Amplification, QTNASBA) techniques are emerging as high-throughput genotyping systems [5]. Multiple marker molecular research can provide insight into the emergence of drug resistance patterns in the field, which can be used to develop malaria control methods. Point mutations in the *P. falciparum* Chloroquine Resistant Transporter *(PfCRT)* and *PfMDR1* genes have been linked to Chloroquine resistance in *P. falciparum isolates, whereas dhfr and dhps have been linked to Sulfadoxine-Pyrimethamine resistance* [6, 7].

Many African countries now use ACTs to treat *P. falciparum* malaria, including Artemether/Lumefantrine and Amodiaquine/Artesunate [8]. Worldwide, *P. falciparum* (malaria parasite) treatment resistance is a serious public health concern [8, 9]. ART-resistant parasites were not linked to the five mutations in some regions, such as Africa [10]. Because of this, it serves as an example of the complexity of the mechanism of *P. falciparum* medication resistance [11]. The only current alternatives for lowering malaria morbidity and death, particularly in Africa, are chemoprophylaxis and chemotherapy in the absence of effective and practicable preventive interventions. As a result, the rising incidence of *P. falciparum* variants resistant to therapies poses significant problem to treating and controlling malaria. Phylogenetics studies the evolutionary relatedness among various groups of organisms through molecular sequencing data and morphological data matrices. In phylogenetics, DNA sequencing methods are used to analyze the observable heritable traits [12]. It also makes use of a phylogenetic tree which is a diagram to show the hypothetical evolutionary histories and relationships of groups of organisms based on the phylogenies of different biological species. The phylogenetic tree has been used to understand biodiversity, genetics, evolutions, and ecology of organisms [12].

This study assessed the prevalence of *Plasmodium falciparum* infection in the South-Western part of Nigeria, the predisposing factors to malaria occurrence, the Artemisinin-based combination therapy resistance in *P. falciparum*, and the molecular variations of *P. falciparum* in the area.

METHODOLOGY:

Study Area and Demographic Data Collection:

The study was carried out in selected Government Hospitals in Ondo and Ekiti States, Nigeria. Ondo State lies between longitudes 4"30" and 6" East of the Greenwich Meridian, 5"45" and 8" 15" North of the Equator. This means that the state lies entirely in the tropics while Ekiti State lays South of Kwara and Kogi State, East of Osun State and bounded by Ondo State in the East and in the South Ekiti State Ethical clearance and approval:

Prior to the commencement of the study, approval was obtained from Selected Government Hospitals, Ekiti State Teaching Hospital, Ado-Ekiti (EKSUTH/A76/2019/04/009), Federal Teaching Hospital, Ido-Ekiti **(**ERC/2018/08/02/131B) and Ondo State Ministry of Health (OSHREC/24/07/19/154). Written informed consent was obtained from each adult participant and the parent or guardian of each child examined.

enjoys tropical weather with two awesome seasons. These are the rainy season (April–October) and the dry season (November–March). This study was carried out from August 2019 to January 2021.

Study Population and Sample Size:

This was a cross sectional Hospital-based study. A total of 399 consented individuals were enlisted into this study. The sampled size was calculated using the following equation:

$n = t^2 \times p(1-p)/ m^2$
Where n = the required sample size, t = confidence level at 95% (standard value of 1.96),
p = estimated prevalence of the infection in the project area which is 71% [13]
m = margin of error at 5% (standard value of 0.05).

$n = 1.9622 \times 0.71(1-0.71)/ (0.05)^2$

$= 3.924 \times 0.2059/0.0025 = 323.180.$

Data Collection:

A structured questionnaire was administered to a total of 399 consented participants from the selected Hospitals in order to collect information on their age, sex, occupation, education, response, and management of malaria. The questionnaire was face validated, pretested, and tested for reliability before administration [13, 14].

Sample Collection and Examination**:**

With the assistance of a trained Medical Laboratory Technician, a sterile syringe was

used to collect 2.0mL of blood from each of the subjects. The blood was put into an EDTA bottle and used for thin and thick blood film preparations. Thin and thick smears of the samples were prepared on sterile slides and subsequently stained with Giemsa stain. The smears were viewed under an x100 objective lens of the light microscope to detect the presence of malaria parasites [13, 15].

Molecular characterization of *Plasmodium falciparum*:

The DNA were extracted using commercial kit (Norgen Biotek Corp, Canada) and the purified genomic DNA samples were then eluted into separate properly labeled microcentrifuge tubes and stored at 4^{o}C until required for analysis.

Plasmodium falciparum species specific primers, vacuolar proton adenosine triphosphate (vapA) gene (Table 1) was used to amplify the genomic DNA and was followed by sequencing, blast, alignment and phylogenetic tree analysis using MEGA - X [16].

Molecular Identification of Antimalarial Resistant Genes (Nested PCR):

The gene fragment of *Plasmodium falciparum kelch-13* resistance gene (*Pfk-13*- PCR- F- CGG AGT GAC CAA ATC TGG GA; PCR- R- GGG AAT CTG GTC GTA ACA GC) as shown in table 1 was amplified by nested PCR protocols reported previously [17]. The products of restriction digestion were separated by electrophoresis on a 2% agarose gel and detected by staining with ethidium bromide which were sized 1- kilo base pair (2000bp) molecular weight marker (New England Biolabs, Beverly, MA). The bands were identified at 2000bp for successful amplifications. The experiment was done at the (Bioscience Centre, International Institute of Tropical Agriculture, Ibadan, Nigeria).

Table 1: Primer Sequence

Primer Name	Primer Sequence	Amplicon size (bp)
Pfk-13- PCR F- PCR- R- [16]	5'- CGG AGT GAC CAA ATC TGG GA -3'; 3'- GGG AAT CTG GTC GTA ACA GC- 5'	2000
VapA (vacuolar adenosine trisphosphate) L08200.1- F-, R- Bunmi Obagaye, 2016- unpublished)	5'CTTCTTATTACGGAGCAAAATGACA 3' 3'CCACAACCAAATGCACCAGG 5'	750

Statistical Analysis:

The data were analyzed using IBM Statistical Product and Service Solutions (SPSS) version 23 which was used to determine the differences in prevalence of malaria by age, sex, occupation, education, frequency, response and management of malaria. The results were expressed as mean ± standard error of mean (SEM). Significant differences were established by the one-way analysis of variance (ANOVA). Mean values with $p<0.05$ were considered statistically significant.

A total of 80 samples were extracted and amplified using vacuolar Adenosine trisphosphate (vapA) gene primer. About 55 (68.75%) out of the amplified samples showing clear bands at 750bp were sequenced and analyzed for the molecular detection of *Plasmodium falciparum* as shown in Plate 1.

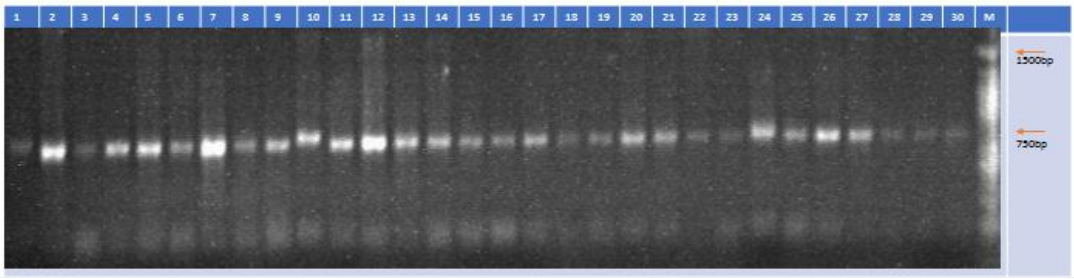

Plate 1: Amplified *P. falciparum* using vacuolar adenosine trisphosphate (vapA) gene
Key: M showing the ladder

equence Blast of Isolated *Plasmodium falciparum:*

Twenty- five (25) strains of *P. falciparum* were identified following sequence blast of isolates as shown in Table 2. Isolates 3, 11, 17, 18, 19 and 20 showed 100% homology to the nearest relatives compared with Isolates 10, 23a, 36, and 42 recorded 99% homology relationships. Isolates 13, 22, 26a, 28a, 34, 23b, 24, 25b, 26b, 27, 28b, 29 and 30 showed 98% homology while isolate 25a showed 97% relationship with existing isolate (Table 2).

Table 2: Nearest relatives of isolated *Plasmodium falciparum* following sequence blast

S/N	Isolate code	Nearest relatives	Accession no	Homology
1	6	*Plasmodium falciparum* Strain BAK5	DQ135202.1	100%
2	10	*P. falciparum* Strain BK71	KY337745.1	99%
3	13	*P. falciparum* Strain 0957	AM116507.1	98%
4	17	*P. falciparum* Strain BAK27	DQ135134.1	100%
5	20	*P. falciparum* Strain BK543	KY331903.1	100%
6	22	*P. falciparum* Strain 0886	AM116315.1	98%
7	23a	*P. falciparum* Strain BK820	KY337016.1	99%
8	25a	*P. falciparum* Strain 445	KP086191.1	97%
9	26a	*P. falciparum* Strain BK959	KY332967.1	98%
10	28a	*P. falciparum* Strain 37F3-17	KC678236.1	98%
11	34	*P. falciparum* Strain F1 EMP-1-	MT017271.1	98%
12	36	P. falciparum Strain Bk622	KY333674.1	99%
13	42	*P. falciparum* Strain BK 753	KY335857.1	99%
14	11	*Plasmodium falciparum Strain TH166.12*	MT060894.1	100%
15	15	*P. falciparum Strain PO19*	DQ135473.1	98%
16	18	*P. falciparum Strain DO-39*	KC887581.1	100%
17	19	*P. falciparum Strain PIK20*	HQ733544.1	100%
18	23b	*P. falciparum Strain GC27*	KX849839.1	98%
19	24	*P. falciparum Strain GC38*	KX850025.1	98%
20	25b	*P. falciparum Strain G3st25*	KX850309.1	98%
21	26b	*P. falciparum Strain GC19*	KX850077.1	98%
22	27	*P. falciparum Strain BK1 309*	KY330890.1	98%
23	28b	*P. falciparum Strain GC20*	KX850697.1	98%
24	29	*P. falciparum Strain GC11*	KX851219.1	98%
25	30	*P. falciparum Strain G3st10*	KX851127.1	98%

Plasmodium falciparum resistant *Kelch-13* gene was detected in 70% of the isolates (Plate 2) after the gel- electrophoresis amplification of the resistant gene.

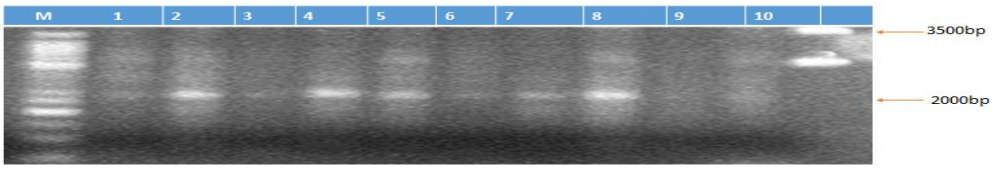

Plate 2: Amplified *P. falciparum* resistant *Kelch - 13* gene
Key: M showing the ladder

Phylogenetic Evolutionary Tree Analysis:

Evolutionary analyses were conducted in MEGAX. Figure 1 showed the phylogenetic tree of the evolutionary relationship of *P. falciparum* isolates from Ekiti and Ondo States. Twenty (25) strains belonging to three clades were identified phylogenetically.

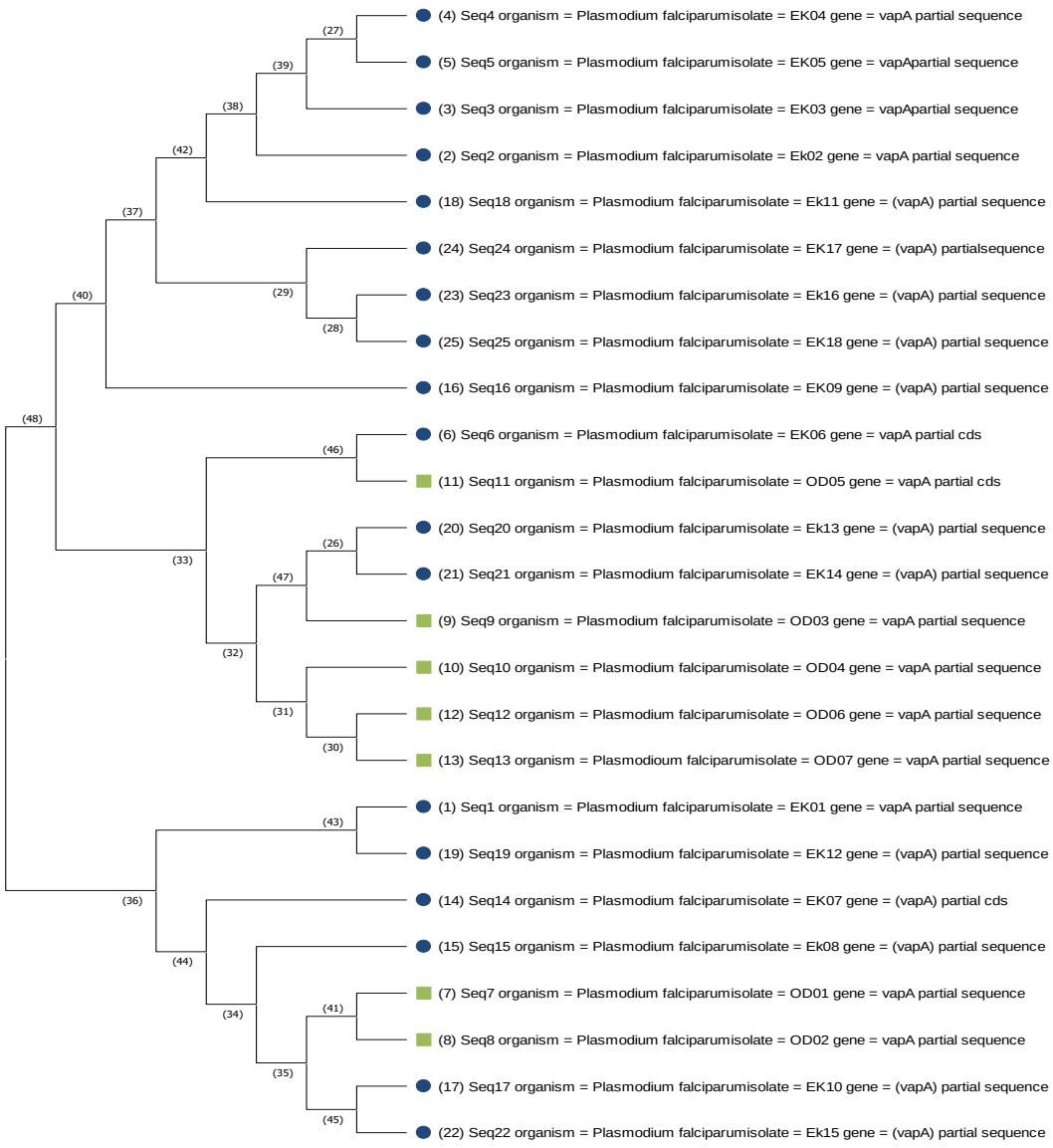

Figure 1: Phylogenetic Tree showing Evolutional Relationship of *P. falciparum* isolates from Ekiti and Ondo States Key: Ekiti - Blue, Ondo – Green

The isolates showed distinct evolutionary relationship when compared to other parts of Nigeria found on National Centre for Biotechnology Information (NCBI) as shown in Figure 2 and 3.

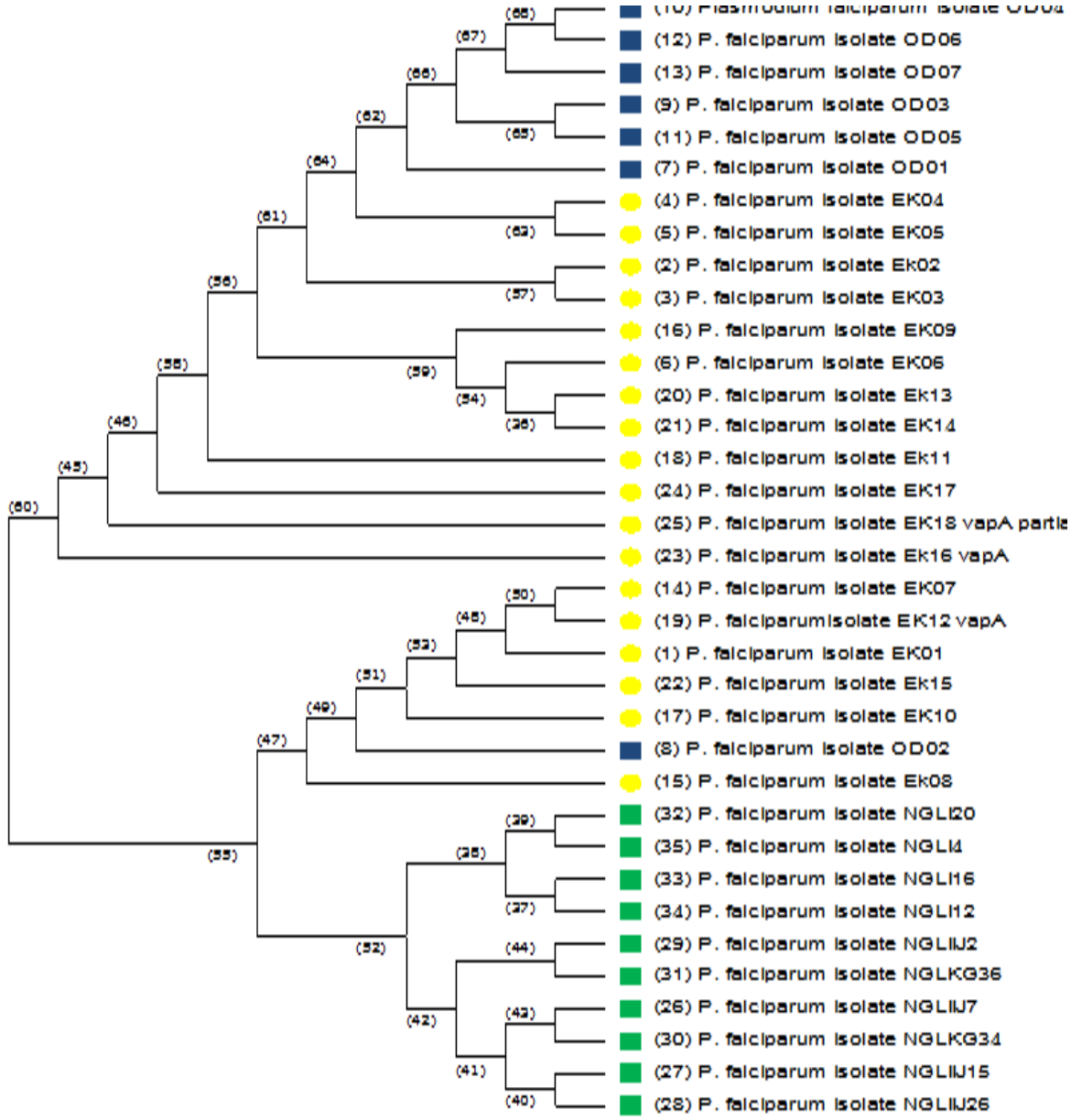

Figure 2: Phylogenetic Relationship of *P. falciparum* isolates from Ekiti, Ondo and other parts of Nigeria.
Key: Ondo - Blue, Ekiti – Yellow, Other parts- Green

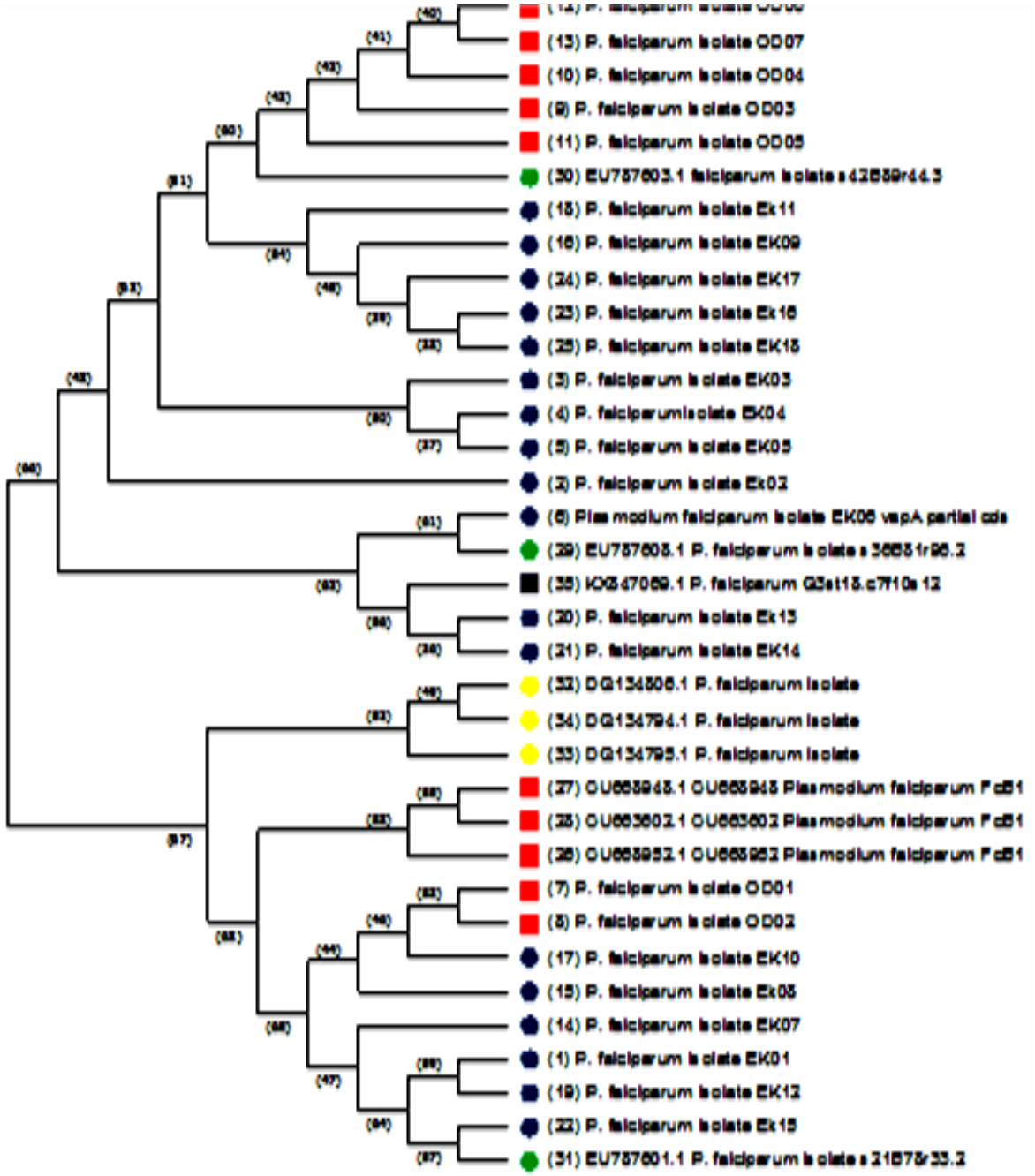

Figure 3: Phylogenetic relationship of *P. falciparum* isolates from Ekiti, Ondo and other parts of the World.
Key: Ondo - Red, Ekiti – Blue, Uk- Green, New Guinea – Yellow, France – Orange, South America – Purple.

DISCUSSION:

The efficacy of ACTs is being monitored in most malaria-endemic countries. There have been some reports of delayed parasite clearance during routine therapeutic efficacy studies of ACTs conducted in Africa. However, these reports have not been consistent over time. Artemether-Lumefantrine and Artesunate-Amodiaquine are the first-line treatment policies used in most African countries, with some countries adding Dihydro - Artemisinin-Piperaquine [11].

This allele was not previously associated with clinical or *in-vitro* resistance to Artemisinin but a study associated it with prolonged parasite clearance in Ugandan children who had severe malaria and were treated with intravenous Artesunate [18]. All the participants in this study tested positive for *Plasmodium falciparum* infection.

The emergence and spread of ACT-resistant isolate in Nigeria is a matter of concern. Looking at the molecular evolutionary pattern in this study, twenty - five different strains of *P. falciparum* were identified and diagnostically, the specific resistant gene primer *K-13* used confirmed the resistance of *Plasmodium falciparum* to ACTs in the study area. Previous research work near the study area [19] confirmed the emergence of resistance to ACTs drugs.

Artemisinin- based Combination Therapy (ACTs) was introduced in 2005 in Nigeria with Artemether–Lumefantrine (AL) as first-line treatment for uncomplicated malaria and Artesunate + Amodiaquine as the alternative [20]. There is no alternative to the current regimen Artemisinin Combination Therapy for the severe uncomplicated malaria. It is essential to monitor the efficacy of the Artemisinin derivative through molecular surveillance study [17]. Recent study aimed to track the research questions raised for the surveillance of *falciparum* infections by the PCR-based sequencing analysis of *Pfkelch13* gene propeller polymorphism [17].

Twenty- five strains of *P. falciparum* belonging to three (3) clades phylogenetically were identified in this study. The isolates from the two States were evenly distributed within the three clades, showing evolutionary relationships. *P. falciparum* resistant *Kelch 13* gene was detected in 70% of the isolates.

This study, though limited to a number of field-sampled malaria parasite isolates and sampled only from Southwestern part of Nigeria, could enlighten on the evolutionary basis of Artemisinin- based combination therapy (ACT) resistance of *P. falciparum*, infection in Nigeria. Considering ACT in different combinations (with Artemisinin being the first-line drug) is the only surviving antimalarial in the control program of

many endemic countries, non-observance of validated AA mutations of *Pfk13* gene with no association among other mutations of other genes conferring resistance to partner drugs is, in fact, welcome news concerning malaria public health situation in Nigeria [21]. However, considering the historical migration of CQ-resistant parasites to Africa from other different malaria-endemic countries e.g., Southeast Asian countries [22] regular and expanded molecular surveillance with a large sample size on the mutations of the *Pfk13* gene are needed to monitor the prevalence of ACT-resistant *P. falciparum* in Nigeria.

CONCLUSION:

Artemisinin Combination Therapy remains the most effective treatment for uncomplicated *falciparum* malaria. Most patients with delayed parasite clearance are cured, as long as the partner drug remains effective.

The Monitoring of the effectiveness of the recommended ACT drugs must be done routinely to ensure timely changes in National treatment policies. More work must be done to study the antigenic shift pattern of *P. falciparum* in their intermediate hosts. In order to prevent antimalarial drug resistance, Plasmodium falciparum antimalarial drug sensitivity should be closely monitored, and compliance with antimalarial drug use should be encouraged in the study area.

Acknowledgement

All the participants and volunteers in this study are well appreciated for their efforts, cooperation and time.

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THE BRIXIA CHEST X RAY SEVERITY SCORE IN ADULT PATIENTS WITH SYMPTOMATIC COVID-19 INFECTION: A USEFUL GUIDE TO MANAGEMENT

Running title: Chest X Ray findings and outcome in COVID-19

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ABSTRACT:
COVID-19 is a highly contagious viral illness with a wide spectrum of clinical manifestations ranging from asymptomatic or mild cold like symptoms to a devastating and often fatal respiratory illness. The elderly and those with underlying morbidity are the groups most often, but certainly not exclusively, associated with death from respiratory pathology. COVID-19 respiratory illness usually manifests clinically as pneumonia with predominant imaging findings of an atypical or organized pneumonia. Chest radiography (CXR) helps to assess the progress of the disease. The BRIXIA score based on radiological appearance may be used to determine the severity and clinical outcome of a patient with COVID-19. The aim of this study was to assess the relationship between the BRIXIA score and the clinical outcome of positive COVID-19 patients at Port Moresby General Hospital (PMGH) in Papua New Guinea (PNG). In this descriptive retrospective study conducted at the Radiology Department of the PMGH the records of 129 Polymerise Chain Reaction (PCR) confirmed patients admitted to PMGH between September and December 2021 were examined. The patients were grouped into mild, moderate or severe categories depending on clinical features at the time of diagnosis. There were 89 (69%) males and 40 (31%) females. The mean (SD) age was 52 (12) years, and the median (IQR) was 53 (44-60). Their admission CXRs were given a Brixia score. Mean (SD) Brixia scores for mild (n=24), moderate (n=67) and severe (n=38) were 4.5 (2.5), 8.9 (2.7) and 12.5 (3.5) respectively. The Brixia score was significantly related to the clinical severity, F 55.49, p <0.001. Twenty seven (77%) of the 35 patients who died had comorbidities of whom 21 (78%) were in the clinically severe group. A Brixia score of 9 or more was closely associated with death, p = 0.001, Odds Ratio with 95% Confidence interval (0R) of 3.9 (1.7-9.6). The Brixia CXR severity score is a useful tool in assessing clinical severity and prognosis in patients with COVID-19.

Key Words: Chest X Ray, Brixia Score, Clinical Severity, Outcome

INTRODUCTION:

Corona virus disease 2019 (COVID-19) is a severe acute respiratory illness caused by SARS-CoV-2, a novel virus belonging to the family Coronaviridae. It was first discovered in December 2019 in Wuhan City, Hubei province in China. It is a highly contagious disease that rapidly spread throughout the world leading the World Health Organization (WHO) to declare a pandemic on March 11, 2020 [1]. The clinical spectrum is wide, with the younger population often asymptomatic or mildly affected with flu like symptoms, but with substantial mortality in the elderly and those with underlying morbidities such as chronic obstructive airways disease and diabetes. A debilitating post viral illness was recognised early in the pandemic [2]. Respiratory pathology remains the main cause of mortality [3].

Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) on nasopharyngeal secretions is the gold standard in diagnosing COVID-19 [4]. Chest x-ray (CXR) is usually of limited value in the diagnosis of early stages of COVID pneumonia when compared to computed tomography (CT) but is very helpful in intermediate to advanced stages of COVID-19 as well as for follow-up. Serial CXRs have been shown to be almost as valuable as CT [5, 6]

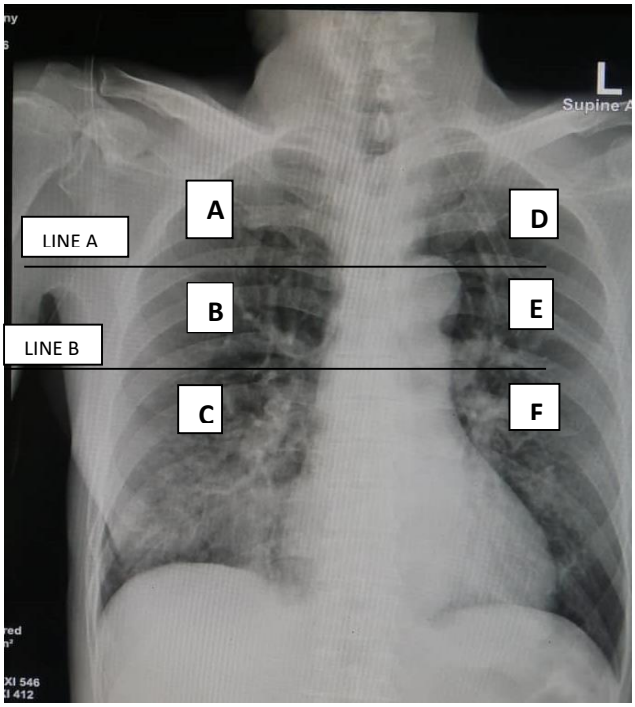
COVID-19 is transmitted via respiratory droplets and as aerosols. In the lungs the virus induces an inflammatory reaction with damage to type 1 and 2 pneumocytes resulting in alveolar collapse and consolidation [7]. The pathophysiological changes within the lung parenchyma are responsible for the radiological features seen on CXR and CT chest as interstitial opacities, ground glass opacities or consolidation.

CXR may be normal in early or mild disease. As the disease progresses, several studies have shown consolidation as the most common finding followed by ground-glass opacities and interstitial opacities. Abnormalities at chest radiography have a peripheral and lower zone distribution with bilateral involvement. Pleural effusion is uncommon [8-10].

Different scoring methods have been used to assess CXR severity of COVID-19, including the Radiographic Assessment of Lung Edema Score (RALES), modified RALES and Brixia score [11, 12].

In calculating the Brixia score horizontal lines drawn at the level of the inferior wall of the aortic arc and a second one above the inferior wall of the right inferior pulmonary vein on frontal projection delineates 6 zones- the right and left upper, middle and lower zones (Figure 1).

Figure 1. The Brixia Score Lung Areas



A score (from 0 to 3) is assigned to each zone based on the lung abnormalities detected as follows:

Score 0: no lung abnormalities;
Score 1: interstitial infiltrates;
Score 2: interstitial and alveolar infiltrates (interstitial predominance);
Score 3: interstitial and alveolar infiltrates (alveolar predominance).

The scores of the six lung zones are added to obtain an overall "CXR SCORE" ranging from 0 to 18. The Brixia score was shown to be related to the likelihood of mortality in 2000 [12].

Our study aimed to assess the use of the Brixia score in our resource restrained setting during a period of high demand on medical imaging services. Ethics approval was given by the School of Medicine and Health Sciences Research and Ethics Committee and permission to carry out the study was granted by the PMGH Administration.

METHODOLOGY:

This descriptive retrospective study was conducted at PMGH, between September and December 2021. Adult patients who tested positive for COVID-19 and had a CXR performed were the target population. Pregnant women and adolescents were excluded.

The CXRs were reviewed with 3 consultant Radiologists. The lung involvement, zonal

predominance and the type of opacity present was identified and the Brixia score for each CXR was calculated and entered into an Excel spread sheet. Hospital record charts were retrieved from the Medical Units and patients' were classified as mild, moderate or severely ill based on their clinical features at the time of the CXR. Patient demographics and underlying morbidities were recorded.

Statistical analysis:

The data was analyzed using the Statistical Package for Social Sciences (SPSS) software version 22. Means and standard deviation (SD) were generated for normally distributed data. Frequencies and percentages were calculated for binary data. ANOVA compared the Brixia scores for each of the clinical groups. The chi-square test and Odds Ratios with 95% confidence limits were used to assess the relationship between Brixia score and outcome using Open Epi.

RESULTS:

PMGH Radiology department registered 363 CXRs for adult PCR positive COVID-19 patients from September 2021 to December 2021. Eighty eight were repeat CXRs to assess the disease progress and 46 cases were not on the Picture Archiving and Communication System (PACS). 229 CXRs were reviewed to determine the common radiological features of COVID-19 (Figure 2).

Figure 2: Recruitment of study cases to determine outcome.

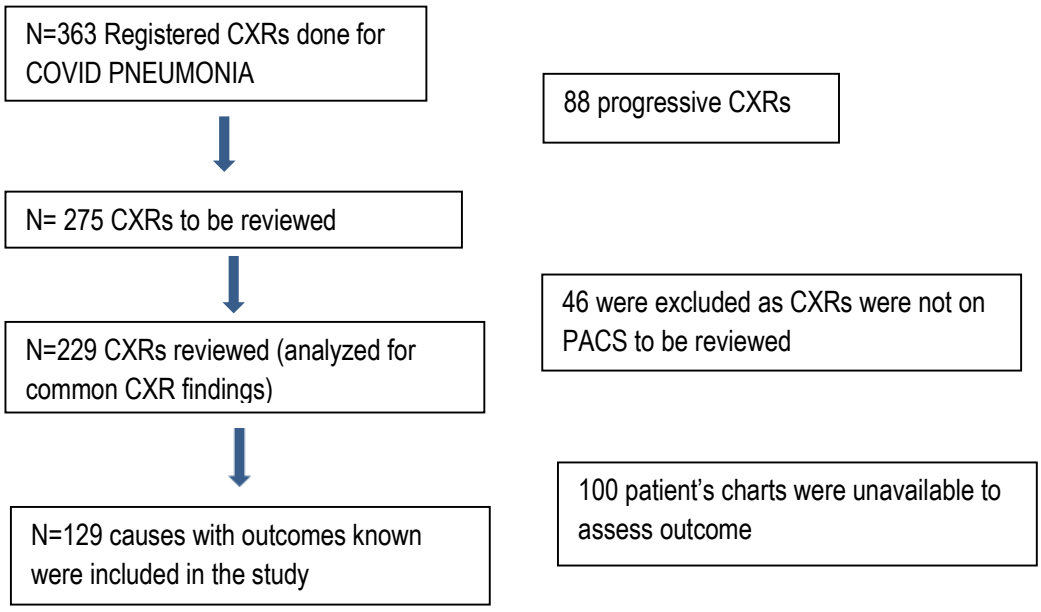


Table 1. Demographic characteristics of 129 COVID-19 patients

Age Years	**Male N (%)**	**Female N (%)**	**Total**
24-34	9 (11.6)	2 (2.5)	11 (14.2)
35-44	15 (19.4)	7 (9)	22 (28.4)
45-54	28 (36.1)	10 (12.9)	38 (49)
55-64	21 (27.1)	16 (20.6)	37 (47.7)
65-74	13 (16.7)	5 (6.4)	18 (23.2)
75-84	3 (3.8)	0	3 (3.8)
Total	89 (69)	40 (31)	129 (100)
≥55	37(41.6)	21 (52.5)	58 (45)
<55	52 (58.4)	19 (47.5)	71 (55)

Table 2: CXR Radiological findings

Radiological findings	Total (n=229)
Affected lung	
Right lung involvement	3 (1.3%)
Left lung involvement	10 (4.4%)
Both lung involvement	212 (93.2%)
Distribution	
Perihilar	23 (10.0%)
Peripheral	108 (47.6%)
Neither	94 (41.0%)
Zone predominance	
Upper zone	0
Mid zone	19 (8.3%)
Lower zone	115 (50.2%)
Non-zonal	91 (39.7%)
CXR opacities	
Ground glass	78 (34.3%)
Consolidation	144 (62.8%)
Interstitial opacities	142 (62.0%)
Pleural effusion	2 (0.9%)
Pneumothorax	1 (0.4%)
Fibrosis	2 (0.9%)
Pulmonary nodules	4 (1.7%)

Table 3: Brixia score and clinical diagnosis Range, Mean (SD)

COVID-19 Severity	Frequency	Brixia score range. Mean (SD)
Mild	24 (18.60%)	Range 0-8, mean 4.5 (2.5)
Moderate	67 (51.9%)	Range 4-16, mean 8.9 (2.7)
Severe	38 (29.5%)	Range 6-18, mean 12.5 (3.5)

Medical case records were retrieved for 129 patients. There were 89 males (69%) and 40 females (31%). For all the 129 patients, the mean age was 52.3 (SD: 12.0) with age range 24-84 years; the median (Interquartile Range: IQR) was 53.0 (44 - 60) years. Table 1 shows the demographic characteristics of all the patients.

Table 2 shows the radiological findings from the initial 229 CXRs reviewed. Both lungs were affected in 214 (93.3%). The opacities were distributed in the peripheral region of the lungs in 108 (47.6%) patients and in the lower zones in 115 (50.2%) patients. Consolidation was present in 144 (62.8%), interstitial opacities in 142 (62.0%) and ground glass opacities in 78 (34.3%).

Table 3 shows the Brixia scores in the mild, moderate and severe clinical groups. There were highly significant differences (ANOVA F = 55.49 p=<0.001) as illustrated in figure 3.

Figure 3: Brixia score and COVID-19 severity

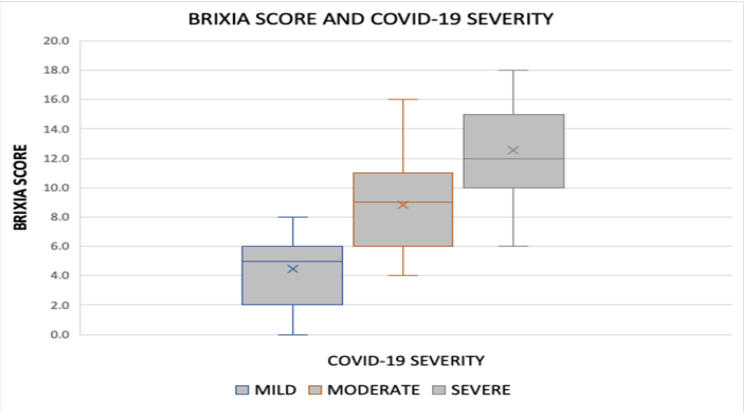


Table 4 shows the outcome in the clinical groups. All patients who died in the clinically mild or moderate groups had underlying comorbidities as did 21 (72%) of the 29 with severe disease at presentation.

Table 4: Outcome of COVID-19 patients

Clinical Severity	Discharged N (%)	Died N (%)
Mild	21 (16)	3 (2)
Moderate	64 (50)	3 (2)
Severe	9 (7)	29 (22)
Total	94 (73)	35 (27)

Table 5 shows the outcome of those with a Brixia score of ≥ 9 and those with a score of <9. Twenty six (39%) of the 66 patients with a score ≥9 died compared with 9 (14%) of 63 who had lower scores. (p=0.001, OR 3.9 (1.7-9.6). There were no differences between males and females in outcome in the two Brixia score groups.

Table 5: Brixia score ≥9 and clinical outcome

Brixia score	**Patients N (%)**	**Deaths N (%)**	**Survived N (%)**
Brixia score ≥9	66	26 (39)	40 (61)
Males	41 (62)	16 (39)	35 (61)
Females	25 (38)	10 (40)	17 (60)
Brixia score <9	63	9 (14)	54 (86)
Males	47 (75)	7 (15)	40 (85)
Females	16 (25)	2 (13)	14 (87)

DISCUSSION:

The COVID-19 pandemic presented many challenges for health services including in the areas of diagnosis and appropriate management. Management decisions can be helped by the availability of accurate and simple prognostic indicators including robust chest radiography algorithms.

There was a male preponderance in our study- consistent with findings from a systematic review and meta-analysis of data from other countries [13]. The review found high frequency of smoking and alcohol consumption in men to be a factor

The most common CXR opacities detected were consolidation 144 (62.8%), followed by interstitial opacities 142 (62.0%) and Ground Glass Opacities 78 (34.3%) consistent with reports from other countries [8-10].

The Brixia scores on the admission CXRs were significantly aligned with the Clinical severity scores with mean (SD) scores for mild, moderate and severe groups of 4.5 (2.5), 8.9 (2.7) and 12.5 (3.5) respectively ($p<0.001$).

The Brixia score was significantly associated with outcome. Twenty six (39%) of 66 patients with a score of ≥9 died compared with 9/61 (15%) patients with a score of <9 ($p=0.003$, OR 3.9 (1.7-9.6). Studies from other countries have reported similar results. In a study of 953 patients in the early months of the pandemic from Lombardy in Italy Brixia scores were significantly higher in patients who died than in survivors $p<0.001$ [14]. In a study from a tertiary hospital in India a Brixia score more than 12 was associated with increased mortality ($p= 0.03$) [15]. Other studies have used combined scoring systems (eg RALES) with the Brixia score or the Brixia score with other risk factors to improve predictive value [16-17].

Our study has a number of limitations. There were no CXRs from non COVID-19 patients with which to compare the Brixia scores performance in predicting outcome in infected patients. The sample size was small, - mainly the result of delay in setting up an adequately documented patient registration system. However, the sample size was sufficient to demonstrate clear associations between Brixia score, severity and outcome. In spite of these limitations the study clearly demonstrated the close association of Brixia score with clinical severity and outcome.

CONCLUSION:

In a resource strained country where CT is limited, CXR is the main radiological modality of choice when dealing with COVID-19. An understanding of the typical CXR features of COVID-19 will aid in diagnosis and monitoring the disease. Our study findings, supported by data from other parts of the world, confirm that the Brixia score is a useful predictor of likely outcome in COVID-19 patients presenting with respiratory signs and can be used to assist clinicians in their management plans.

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FREQUENCY OF TRANSFUSION TRANSMISSIBLE INFECTIONS IN VOLUNTARY AND FAMILY REPLACEMENT DONORS AT THE ALOTAU PROVINCIAL HEALTH AUTHORITY BLOOD TRANSFUSION SERVICE, PAPUA NEW GUINEA

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ABSTRACT:

Transfusion Transmissible Infections (TTI) in blood donors continue to be a threat to recipients, therefore, to increase accessibility to infection-free donor blood, voluntary non-remunerated donation has been recommended. This was a retrospective observational study aimed at establishing a data base for transfusion transmissible infections in family replacement and voluntary donors at the Alotau Provincial Health Authority (PHA) Blood Bank Service using donor data recorded from 2015 to 2018. Statistical significance was determined using the chi-square test with p-values of <0.05 considered significant. Ethical clearance was approved by the School of Medicine and Health Sciences Research Ethics Committee. Consent to collect data from the Alotau PHA Blood Transfusion Service and the Blood Bank Laboratory was granted on the 17/06/2019 reference #: RCO1/6/19. A total of 2852 blood donors were analyzed, of which 90% (n=2567) were males and 10% (n=285) were females. Of these, 69% (n=1959) were Family-Replacement-Donors (FRDs) and 31% (n=893) were Voluntary Donors (VDs). Donations by FRDs increased with increasing years from 2015 to 2017 and declined slightly by 1% in 2018. The complete opposite was observed in VDs. TTIs were higher in FRDs than in VDs (20.1% vs 16.8%, p=0.04), in single infections, (18.6% vs 15.2%, p=0.03), infection with HBV (9.9% vs 7.2%, p=0.02), and in those aged over 45 years (2.7% vs 0.1%, p=<0.01). The differences were statistically significant. TTI was significantly higher in male FRDs than VDs (19.1 vs 14.3, p=0.00) and in females, it was significantly higher in VDs than in FRDs (2.5% vs 1.0%, p=0.00). TTIs were significantly high in older male FRDs which seem to indicate that the primary route of transmission in this setting could be mostly sexual. This calls for establishment of effective educational awareness about risk factors in the older population, and promotion of voluntary non-remunerated donations in this setting.

Key words: Transfusion Transmissible Infections (TTI), HBV. HIV, Syphilis, Family Replacement Donors, Voluntary Donors, Blood Donation.

INTRODUCTION:

Globally, Transfusion Transmissible Infections (TTIs) are higher in Lower Middle-income countries (LMIC) and Low-income countries (LIC) compared to both High Income countries (HIC) and Upper-Middle-income countries

(UMIC) [1]. In the quest to reduce transmission of TTIs through donor blood, the World Health Organization (WHO) recommended 100% Voluntary Non-Remunerated Donation (VNRD) from low-risk individuals in all blood bank settings [2-3]. Although countries have tried to promote this type of donation, Family Replacement Donation (FRD) is still occurring at high frequency. It is as high as 87% in Amman and Jordan [4] to 100% in Northern State of Sudan [5]. FRD may still be necessary especially during acute shortages and emergencies, during which these types of donors are easily accessible.

In addition, because of social [6], cultural practice [7] and religious beliefs [8], potential donors are not willing to give blood voluntarily. In such situation, family members or friends of the patient needing blood often feel obliged to give blood for fear of losing that person from lack of blood transfusion. According to Ehsan et al**.** [9], this type of donors should be encouraged to become voluntary donors to maintain blood supply pools in hospitals. However, in situations where these donors are geographically isolated from the blood bank settings, and only come once in a while when relatives are admitted in hospitals, it can be hard to convert them to VDs because of the distance and also financial constraints they may face.

Compared to the rest of the world, Papua New Guinea (PNG) is one of the countries that has the highest rate of sexually transmitted infections (STIs) [10]. According to a report by the PNG Director for National Blood Transfusion Services, National Department of Health in September 8th, 2022 (11), the current TTI prevalence in PNG is 24.4%, representing about a quarter of wastage of donor blood, 11.4% of which is due to the hepatitis B virus infections [Ref]. Furthermore, the percentage of VD is below 50%; similar to those seen in sub-Sahara Africa [8].

Currently there is no published data on the prevalence of infections among blood donors in Alotau Provincial Health Authority Blood Transfusion Service (APHA BTS); this study was done to establish a data base to help policy makers develop effective strategies to ensure blood safety in this setting.

METHODOLOGY:

Study area**:** The APHA BTS is part of the Alotau Provincial Health Authority Hospital (APHA) which serves the Milne Bay province. It is situated in a maritime location and therefore caters for the many outlying Islands which make up the province of Milne Bay. It has a population of 269 347, served by 188 health centres and aid posts, scattered throughout the province [12], and whose patients are referred to APH Hospital for blood transfusion when in need of blood. Additionally, transportation coverage in the province is 85%, mainly by road and sea.

Study design: This was an observational retrospective study using data collected from the APHA BTS recorded for the year 2015-2018. The information extracted from their archive included the year of donation, age, gender, frequency of donation, type of donation and serological status for Hepatitis B virus (HBs-Ag), Human Immunodeficiency Virus (HIV), Treponema pallidum (TPHA – Treponema pallidum Haemagglutination Test).

Study population: The study population included all donors recorded from January 2015 to December 2018, and who have passed a pre-donation screening procedure before donation. This includes screening of haemoglobin (HB) level, weight (wt), blood pressure (BP), and pulse rate (PR), medical history including social status.

Data Analysis: All data were entered and analyzed in Excel program (Microsoft Office 2010 version). Statistical significance between categorical variables was calculated using the chi-square test, 95%CI was calculated for prevalence and a p-value of 0.05 was considered significant.

Ethical approval: Ethical clearance was obtained from the University of PNG (UPNG) School of Medicine and Health Sciences (SMHS) Research Ethics Committee. The consent to collect data from the Alotau Provincial Health Authority was granted on the 17/06/2019 reference #: RCO1/6/19 by the APHA Research Ethics Committee.

RESULTS:

In this retrospective study, data for a total of 3071 blood donors were collected from archived records at the Alotau Provincial Hospital Blood Transfusion Services from 2015 to 2018. Of these, 7% (n=219) were excluded. Thus, the data for 2852 blood donors were analysed. Of those that were analysed 31% (n=882) were donated in 2015, 25% (n=711) in 2016, 24% (n=695) in 2017, and 20% (n=564) in 2018. In these four years period, 90% (n=2567) donors were males and 10% (n=285) were females (Table 1).

From 2015-2018, the total number of Family Replacement Donors (FRDs) were 69% (n=1959) and Voluntary Donors (VDs) were 31% (n=893). Of the FRDs, 63% (n=1800) were males and 6% (n=159) were females. Of the VDs, 27% (n=767) were males and 4% (n=126) were females. In both groups, male donors comprised the majority of the donors.

The mean age of all the donors was 32.4 ± 10.1 years and the age range was 16 - 87 years. The donors in the 30 years age group frequently donated blood during the study period, in the overall population and also among males and FRD donors. Female donors in the 28 years age group frequently donated blood compared to the

other age groups. In VDs, females in the 32 years age group frequently donated.

Over the four-year period, male donations steadily increased from 87% in 2015 to 93% in 2018, while female donors declined from 13% to 7% in the same period (Table 1). In the same way, FRD donations steadily increased from 53% in 2015 to 82% in 2017 but slightly declined to 81% in 2018, while VDs steadily declined in the same period to 2017, and in 2018, a slight increase to 19% was observed. These changes are illustrated in Figure 1.

A significant difference in TTIs was observed between FRDs and VDs (20.1% vs 16.8%, *p*=0.037 respectively). The same scenario was also observed in single infections (18.6% vs 15.2%, *p*=0.027) with HBV (9.9% vs 7.2%, *p*=0.021), males (19.1% vs 14.3%, *p*=0.02) aged over 45 years old (2.7% vs 0.1%, *p*=<0.001) respectively. Transfusion transmissible infections were significantly high in female voluntary donors than FRDs (2.5% vs 1.0%, *p*=0.003) respectively (Table 2). Single infections with HIV and syphilis, dual and triple infections showed no significant difference between FRDs and VDs (Table 2).

Table 1: Annual distribution of blood donors by gender at APH BTS from 2015 – 2018

Years	Total Donors	Females % (n)	Males % (n)
2015	882	13% (118)	87% (764)
2016	711	11% (79)	89% (632)
2017	695	7% (48)	93% (647)
2018	564	7% (40)	93% (524)
2015 - 2018	2852	10% (285)	90% (2567)

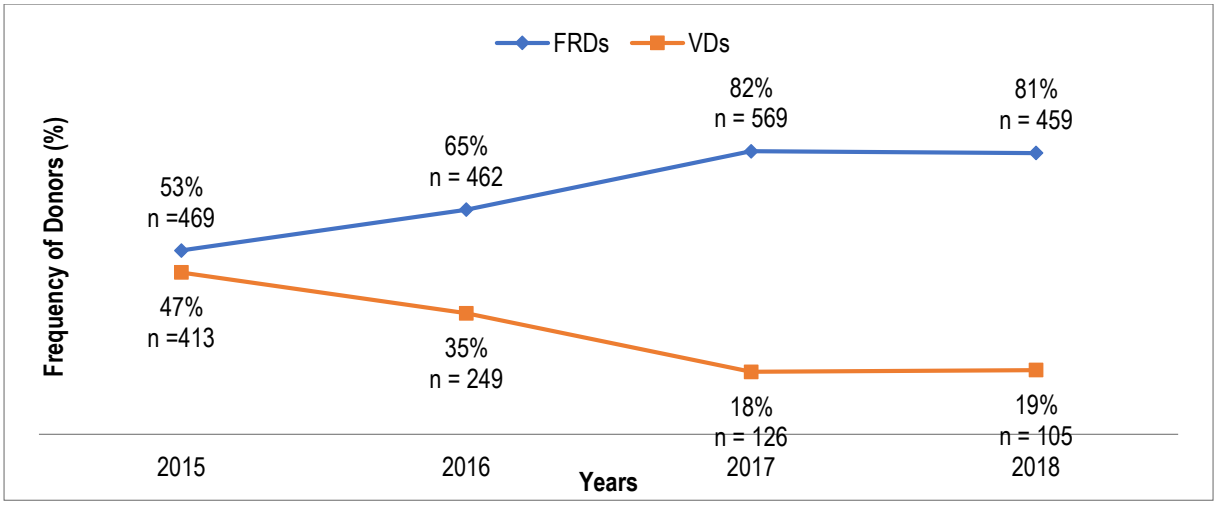

Figure 1: Annual distribution of FRDs and VDs at APHA BTS from 2015 – 2018, Milne Bay Province, Papua New Guinea. FRDs is showing a steady increase from 2015 to 2017 and slightly declined in 2018, while VDs showed a decline in the same period and a slight increase in 2018.

Table 2: Distribution of 2852 donors according to the prevalence of infection with TTIs among FRDs and VDs.

	FRDs (n=1959)		VDs (n=893)			
	Proportion Positive	Prevalence (%)	Proportion Positive	Prevalence (%)	X^2	p=value
	(%)	95%CI	(%)	95%CI		
Total # of TTIs	394	20.1 (18.3-21.9)	150	16.8 (14.4-19.3)	4.367	0.04
Single Infection	365	18.6 (16.9-20.4)	136	15.2 (12.9-17.6)	4.90	0.03
HBV	194	9.9 (8.6-11.2)	65	7.2 (5.6-9.0)	5.3	0.02
HIV	25	1.3 (0.8-1.8)	9	1.0 (0.4-1.7)	0.38	0.54
SYPHILIS	145	7.4 (6.2-8.6)	63	7.0 (5.4-8.7)	0.11	0.74
Dual Infection	29	1.5 (1.0-2.0)	14	1.6 (0.8-2.4)	0.03	0.86
HBV/HIV	2	0.1 (-0.0-0.2)	3	0.3 (-0.0-0.7)	1.92	0.17
HBV/SYPHILIS	24	1.2 (-0.7-1.7)	11	1.3 (0.5-2.0)	0.00	0.99
HIV/SYPHILIS	2	0.1 (-0.0-0.2)	0	0.0 (0.0-0.0)	0.91	0.34
Triple Infection	1	0.1 (-0.1-0.2)	0	0.0 (0.0-0.0)	0.46	0.5
Sex						
Males	374	19.1 (17.4-20.8)	128	14.3 (12.0-16.6)	9.57	0.00
Females	20	1.0 (0.6-1.5)	22	2.5 (1.5-3.5)	8.80	0.00
Age-Group						
15-29	169	8.6 (7.4-9.9)	88	9.9 (7.9-11.8)	1.13	0.29
30-44	172	8.8 (7.5-10.0)	61	6.8 (5.2-8.5)	3.11	0.08
≥45	53	2.7 (2.0-3.4)	1	0.1 (-0.1-0.3)	22.21	<0.01

DISCUSSION:

The results showed 9 to 1 ratio of male to female donors during the study period. Similar studies done in different parts of India reported similar ratios of male to female donors [13-14], however, this is in contrast to Mamu and Varpit [15] whose study showed a lower male to female ratio of 4:1. The low number of donor population and type of donor selection in this latter study could be the reason for its low ratio. However, male donor dominance in all of these studies is similar, possibly due to their willingness to donate blood compared to females [16]. Moreover, the trend of male donations in this current study increased with increasing years, while female donors showed an opposing trend (Table 1). A study done in Port Moresby General

Hospital Blood Transfusion Service (PMGH BTS) in PNG, also showed a similar trend [15]. No explanation was offered for this scenario; however, the low number of female donors could be attributed to their low haemoglobin level reported in 1983 by Talonu [17] at PMGH BTS in PNG, or it could be due to social factors such as ignorance, social taboos [18] or normal physiological reasons such as child bearing age, pregnancy and menstrual flow [19], or religious and cultural beliefs [7-8].

Over the four years period of the current study, the proportions of FRDs steadily increased from 53% in 2015 to 82% in 2017 and in 2018, it slightly declined by 1%. On the other hand, the proportions of VDs declined with increasing years from 47% in 2015 to 18% in 2017, and then slightly increased to 19% in 2018. The decline of VDs to 17% in 2017 (Fig 1) was probably due to theft; blood bags were stolen from the blood bank during the year and were not retrieved. This may have caused fear in VDs, which may have induced family members and friends to donate more frequently for family members and friends in the hospital for fear of losing them. Another reason for the decline in voluntary donation could be lack of effective awareness campaign drives to promote voluntary donation, because of geographic isolation of these islands from the main blood collection centre. These are of course assumptions which should be substantiated by further research.

The prevalence of TTIs in this study was significantly high in FRDs than in VDs (20.1% vs 16.8% p=0.04); especially prominent in FRD males (19.1%, p=0.00), and those over 45 years old (2.7%, p=<0.01); although among female donors, it was significantly high in VDs (2.5% vs 1.0%; p=0.00) (Table 2). This finding is similar to Mohamed *et al.* [20] who reported TTIs to be twice as high in FRDs (9.0%) as compared to VDs (4.0%). Similarly, in Eritrea [21], in Egypt [19] and at PMGH BTS in PNG [14], high TTI proportions were reported in FRDs; all of which were however, in contrast to the findings of Siraj *et al.* [22] and Varpit & Malana [23], who reported high TTI frequencies in VDs. This could have been due to the high numbers of VD donor populations and also the study duration in the latter two studies, whose studies included data collected over longer periods of time.

However, in this current study, most of these FRDs come from the outlying Islands in Milne Bay province and therefore they either do not always go back to the blood transfusion centre to collect their results, or are not notified of their serological status. This is similar to a study in Tanzania who, despite reporting high TTI prevalence, only less than 10% of the donors positive for TTIs were notified of their results [20], owing to lack of resources, inadequate contact and difficulties encountered by individuals having to travel long distances. These factors could have applied to donors in this present study, given the geographic

isolation of the donors. However, this remains to be substantiated by further prospective study to look at possible reasons, and to develop ways of reaching out to these Islands to promote voluntary unpaid blood donation.

The global prevalence of TTIs in blood donations categorized according to income groups is reported to be higher in Lower middle-income (LMIC) and Low-income countries (LIC), compared to High-income (HIC) and Upper middle-income countries (UMIC) [1]. Because of the risk of transmission of TTI through blood transfusion, the WHO recommends collection of blood from low-risk, regular and voluntary unpaid donors. It is quite disturbing that this is contrary to this current study in which the majority are FRDs.

Single infections were higher in FRDs as compared to dual infections which were slightly higher in VDs, however the difference was not statistically significant (1.6% vs 1.5%, p=0.86) respectively (Table 2). This is similar to a study done in Eritrea who found the odds of FRDs being contaminated with at least one TTI to be high (OR=1.56, 95%CI 1.10-2.21 [24].

The significantly high TTI rates in male FRDs, female VDs and in the older population (Table 2) seen in this current study could be due to lack of adequate understanding of the risks of TTIs among the older population as demonstrated by Keleta *et al.* [24]. In fact, the mean age for FRDs and VDs in this current study indicates an older population (32.8±9.7 years and 31±11 years) respectively, suggesting that the modes of TTI transmission is more likely to be sexual.

In single infection, TTI with the hepatitis B virus was significantly high in FRDs than VDs (9.9% vs 7.2%, p=0.02). The high prevalence of HBV infection in FRDs in this study is in concordance with Ahmed *et al.* [25] and Mohamed et al. [20] but in contrast to other studies [26-27], who reported statistically insignificant differences in HBV infections between FRDs and VDs. Although HIV and syphilis infections were higher in FRDs compared to VDs in this study, the difference in infection between the two was not statistically significant (1.3% vs 1.0%, 0.54; 7.4% vs 7.0%, p=0.74) respectively. However, according to a study in Tanzania [28], FRDs were reported to be 1.22 times more likely to be detected with HIV than VDs, and 1.35 times more likely to be detected with HBV infections than VDs. Additionally, male donors were 1.19 times more likely to be positive for syphilis than females. Similarly, another study [15] reported a lower risk of VDs being infected with HBV (OR = 0) and syphilis (OR =0.9) than FRDs, although the risk of VDs being positive for HIV was high (OR = 1.16, 95%CI 0.813-1.65). These results suggest the need to promote voluntary non remunerated donations and strict adherence to thorough pre-screening protocols during pre-donation screening to reduce the window period and thus increase safety to recipients.

CONCLUSION:

Transfusion transmissible infections are prevalent in blood donors in MPHA BTS and are significantly high in male FRDs, female VDs and in the older population (over 45 years old). Single infections with HBV are significantly higher than dual and triple infections. This calls for establishment of effective educational awareness about the risks of infection among the older population, and promotion of voluntary non remunerated donations among the population in this area is paramount.

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ASSESSING THE IODINE STATUS OF CHILDREN, AVAILABILITY AND AWARENESS OF IODISED SALT, USE OF SALTY CONDIMENTS AND FLAVOURING IN HOUSEHOLDS IN ZIA COMMUNITY, HUON DISTRICT, MOROBE PROVINCE PAPUA NEW GUINEA

Running title: Iodine status of children and iodised salt use in remote communities in Papua New Guinea

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ABSTRACT:
The strategy of fortifying food grade salt with iodine has been globally successful in increasing iodine intake and significantly reducing the prevalence of iodine deficiency. In addition, the consumption of salt through processed foods is increasing in many countries. The major objectives of the current study were to assess the iodine nutritional status among school children, the availability and awareness of iodised salt, the use of salty condiments and flavourings in households in a remote Zia community. This was a school and community based prospective cross-sectional study carried out in February 2020. The study population included 6 to 12 years old school children in five schools in Zia. Simple random sampling was used to select the children. Salt samples were collected from randomly selected households in the community. Discretionary salt intake was also assessed in a sub-set of households. The size of the thyroid gland of the children was assessed by a single specialist endocrinologist using the standardized procedure for palpation and grading, after which a single urine sample was collected from the children after obtaining informed consent from their parents. A pre-tested questionnaire was used to assess the awareness and use of iodized salt in the households. The iodine content in salt samples was measured using the single wavelength semi-automated WYD Iodine Checker Photometer. The urinary iodine concentration (UIC) was measured by isotopic dilution, using ^{129}I as a spike. The $^{127}I/^{129}I$ ratio was measured by Inductively Coupled Plasma Mass Spectrometry (ICPMS) (quadrupole ICP-MS iCap). The volume of urine required per run was 0.3ml. The mean iodine content of the salt samples from the Households was 31.7 ± 5.9mg/kg. The daily per capita discretionary intake of salt was 5.7 ± 2.2g. The calculated per capita discretionary

intake of iodine was 126.5 ± 48.8µg per day. The Median UIC among the children was 147.5µg/L, which indicates normal iodine status at the time of this study. A total of 44.5% of all the children had palpable goiter (grade 1). This may indicate long-standing prevalence of mild status of iodine deficiency. Majority of the households (93.9%) used Maggi Kakaruk stock cubes to make their food salty compared to 90.9% that used salt. Instant noodles/2-minute noodles are the best wheat based alternative processed foods that should be fortified with iodine. Salt and Maggi Kakaruk stock cubes are the two optimal food vehicles for fortification with iodine in this remote community.

Keywords: Iodine deficiency, school children, Zia community, salty condiments

INTRODUCTION:

Iodine deficiency disorders (IDD) refer to the effects of iodine deficiency (ID) on growth and development, particularly brain development that can be prevented by adequate intake of iodine at the appropriate time [1]. This reconceptualization has been one of the major factors in securing much more attention to the problem of ID over the past decade.

ID is the preventable cause of mental retardation in communities with suboptimal intake of iodine [1, 2]. The occurrence of severe ID that leads to endemic cretinism has been significantly reduced in many countries as a result of dietary iodine supplementation programs [1, 2]. However, mild to moderate (sub-clinical) ID still persists in some countries, especially the subtle degrees of mental impairment, which occur in apparently healthy children with suboptimal dietary intake of iodine [1, 2]. The mean IQ of a community with low intake of dietary iodine may be reduced by 10-15 IQ points. The consequences may include decreased educability, apathy and reduced work productivity, leading to impaired social and economic development [1, 2].

The main intervention strategy for prevention and control of ID is universal salt iodization (USI). It is the paramount strategy, as universal underlines the importance that all salt for human consumption, including that which is used in processed foods, and that used for animal consumption be iodized [1 – 4]. The strategy of fortifying food grade salt with iodine has been globally successful in increasing iodine intake and significantly reducing the prevalence of ID. In addition, the consumption of salt through processed foods is increasing in many countries [5, 6]. If the salt contained in such foods is adequately iodized, it can be an important source of iodine [5, 6]. National salt iodization programs should encourage and monitor the use of iodized salt in processed foods.

The USI strategy was implemented in Papua New Guinea (PNG) in June 1995 with enactment of the PNG Salt Legislation, which prohibits the importation and sale of non-iodized salt [7, 8]. According to the findings of the 2005 PNG National Nutrition Survey (PNG NNS 2005), 92.5% of the salt samples from households were adequately iodized [9]. In addition, iodine status was adequate among non-pregnant women of child-bearing age, with median urinary iodine concentration (UIC) of 170µg/L. This indicated that the USI program has been successful in achieving good coverage in urban and accessible rural areas [9].

Mini-surveys [10 – 14] on iodine status carried out after the PNG NNS reported prevalence of mild to moderate status of iodine deficiency among School-age-children (SAC) in Aseki-Menyamya district Morobe province, Lufa district Eastern Highlands province, Karimui-Nomane district and Sina-Sina Yonggomugl districts in Simbu province. Some of these areas are in remote mountainous regions. These studies also reported that the communities have limited access to commercial salt, some of which was not adequately iodized, and there was limited knowledge about the importance of using iodized salt and the consequences of ID on health outcomes. These authors indicated the need for further assessment of the iodine status among the vulnerable communities in the other remote mountainous areas in the country.

The major objectives of the current study were to assess the iodine nutritional status among school children, the availability and awareness of iodised salt, the use of salty condiments and flavourings in households in the Zia community in Huon district Morobe province in PNG. This was done by determination of the discretionary per capita intake of salt per day, the availability of adequately iodised salt, the iodine status of school children (age 6 –12 years) and the use of a questionnaire to assess the use of salty condiments and flavourings in the households.

METHODOLOGY:

Study site and Population: The study was carried out in Morobe Province, which is one of the four provinces in the Momase region in PNG. The province is made up of nine districts: Bulolo, Finschhafen, Huon, Kabwum, Lae, Markham, Menyamya, Nawae and Tawae-Siassi [15].

Zia is located in the Huon district Morobe rural Local Level Government (LLG). The Zia tribal area covers the lower reaches of the Waria Valley and extends along the Solomon Sea north and south of the river mouth. Communities include Zare, Ainse, Siu, Popoe, Dona, Saigara, Pema, Siu, Bau and Eu [15]. They are located about 165 km south-east of Salamaua rural LLG on the social political and ethnic boundary of Oro and Morobe Provinces.

Zia is a remote area. Topography is rough and rugged with poorly developed infrastructure and poor roads, small valleys and flat lands for large cash crops. The Waria River (major one) and its tributaries are fast flowing and swift in washing downstream all that is in their way.
Major mode of transport from Lae city (Capital of Morobe province) to Zia is by motor-boat (dinghy), it takes about seven hours on a dinghy plus about 24 hours working along rugged paths and small valleys.

Staple foods are taro, banana, sweet potato and sago. Some of these food items cannot be grown in the area because of the extensive soil erosion and climate change.

The population is 10,000 to 15,000. Administrative Centre is Morobe for the Zia and four other neighbouring communities: Yekora and Suena to the north of Zia territory, Binadere to the south-east and Mawae to South-west. Of the four, Zia is the largest and dominant tribal group in the Zia area. The Zia speak the language of the same name - Zia, but Tok-Pisin, limited English and some Kote - a church lingua franca is spoken among older people. Among the Zia, the education is generally poor, literacy is very low, worst among girls and women. Health indicators are generally poor, all village aid posts were closed at the time of this project, and this was due to lack of medicine except for the Zaka sub-health centre. The people rely very heavily on traditional herbs and traditional medicine [15].

Sample size: A sample size of 390 school children was targeted for this study based on the Guidance proposed by UNICEF for the Monitoring of Salt Iodization Programmes and Determination of Population Iodine Status [3]. Recognizing that typical samples size calculations cannot be undertaken for median UICs the UNICEF Guidance notes "*Research indicates that around 400 urine samples per population group are required to measure the median UIC with 5% precision and 100 urine samples to measure the median UIC with 10% precision*." Thus, a sample size of 390 with a response rate of 90% was considered adequate to provide sufficient precision in this small-scale study with limited resources.

Study design and sampling: This was a school and community based prospective cross-sectional study carried out in February 2020 among the Zia community in Huon district Morobe rural LLG. During the pre-visit to the site a list of all the schools and houses was prepared. The schools and houses were randomly selected and the age of children recorded. Five schools participated in this study. Simple random sampling was used to select the consented participants for the study. Informed consent was obtained from the appropriate

authorities in the communities, schools and households.

A pre-tested questionnaire was used to assess the awareness and use of iodized salt in the households. The questionnaire was given out to the parents/guardians/elders of households to fill at the time of urine collection.

Collection of samples**:** The major objectives of the study were explained to the community leaders, the head of each school and to the teachers, with a request for them to communicate the information to the parents and guardians of the children.

To assess the availability of salt, households were randomly selected. A teaspoon of salt was collected from the salt available in each household and placed in a labelled zip-locked bag**.**

To determine the discretionary intake of salt, sealed packets containing 250 g of iodised table salt were distributed to randomly selected households. The number of individuals living in each household and eating food from the same cooking pot/hearth was counted and recorded. The head of the household was requested to use the salt as usual for cooking and eating. Each household was visited three days later to determine the amount of salt remaining in the packet. The number of individuals living in each household was again counted and recorded. The data obtained was used to estimate the average discretionary intake of salt per capita per day.

For the determination of Urinary Iodine Concentration (UIC), single urine samples were collected at the school from each of the selected school children, after obtaining informed consent from their parents or caregivers. Each urine sample was kept in a properly labelled sterile plastic tube with a tight-fitting stopper that was further sealed with special plastic band.

Assessment of thyroid gland by palpation:

The size of the thyroid gland was assessed by a single specialist endocrinologist using the standardized procedure for palpation and grading of the thyroid size [1]. The non-palpable goitre was grade 0; palpable but not visible goitre was grade 1; palpable and visible goitre was grade 2.

The size of the thyroid gland changes inversely in response to alteration in iodine intake, with a lag interval that can vary from a few months to several years [1]. The prevalence of goitre is an index of the degree of longstanding iodine deficiency and therefore is less sensitive than median UIC for the evaluation of a recent change in the status of iodine nutrition in a population [1].

Palpation was used in the present study because ultrasonography is cumbersome and

very expensive to carry out in remote areas, especially in resource limited countries. Palpation is the simple acceptable alternative when carried out by a specialist endocrinologist.

Questionnaire on availability and awareness of iodised salt, use of salty condiments and flavourings:
The modified questionnaire used in an earlier study [14, 16] was pre-tested among 25 randomly selected households in Port Moresby. Feedback and suggested changes were provided orally and in writing. This feedback was used to adapt and improve the questionnaire. It was then used in the present study.

The salt samples, urine samples and questionnaires were transported by airfreight to the Micronutrient Research Laboratory (MRL) in the School of Medicine and Health Sciences (SMHS) University of Papua New Guinea (UPNG) for analysis.

Exclusion criteria: All children below 6yrs of age and above 12yrs of age were excluded from the study. Urine samples were collected only from children whose parents or guardians gave consent.

Assay of salt and urine samples: The quantitative assay of iodine content in salt from the households and trade stores was carried out using the WYD Iodine Checker [17]. Each of the salt samples was assayed three times. The Westgard Rules using Levy-Jennings Charts were used for internal bench quality control (QC) for daily routine monitoring of performance characteristics of the WYD Iodine Checker. The Percent coefficient of variation (CV) ranges from 2.5% to 5.0% throughout the analysis.

For quantitative assay of urinary iodine concentration (UIC), aliquots of the urine samples were sent via courier service to the Human Nutrition Laboratory, Institute of Food Nutrition and Health, ETH Zurich, Zurich, Switzerland. The UIC was measured by isotopic dilution, using ^{129}I as a spike. The $^{127}I/^{129}I$ ratio was measured by Inductively Coupled Plasma Mass Spectrometry (ICPMS) (quadrupole ICP-MS iCap). The volume of urine required per run was 0.3ml [18].

Data analysis and interpretation**:** The Statistical Package for Social Sciences (SPSS) software (version 21 for Windows) and the Microsoft 365 Excel Data Pack were used for statistical analyses of the data. Shapiro-Wilks test was used to assess normality of the data. Mann Whitney U and Wilcoxon W tests were used for differences between two groups; Kruskal-Wallis and Friedman were used for comparison of all groups. A p-value of < 0.05 was considered as statistically significant.

The criteria used for interpretation of the salt iodine data were based on the PNG salt legislation [7, 8]. According to the legislation all salt must be iodised with potassium iodate; the amount of iodine in table salt should be 40.0 to 70.0 ppm (mg/kg); the amount of iodine in other salt should be 30.0 to 50.0 ppm. These levels of iodine should be present at production or import level. WHO recommendations for iodine levels of food grade salt aim to provide 150 μg iodine per day, assume 92% bioavailability, 30% losses from production to household level before consumption and variability of ±10% during iodisation procedures [4]. If 30% of iodine is lost from salt iodised per PNG food regulations, iodine content of table salt at household level should be at least 28 ppm (40 ppm minus 30%). This implies that in PNG the iodine content in salt in retail outlets or at the time of consumption should be at least 28.0 ppm [7, 8]. A cut-off of 30.0 ppm has been used in the analysis of this study by rounding up this figure. Global norms for iodine levels of salt at household level are 15 ppm based on the assumption that average salt consumption of 10 g per day would provide the adult iodine requirement of 150 μg per day [1]. Salt with iodine levels of less than 5 ppm is considered non-iodised salt [3].

For the UIC data, the recommended WHO/UNICEF/ICCIDD (IGN) criteria were used to characterise the status of iodine nutrition among the school children [1]. According to the criteria, a population of school-age children is considered iodine deficient if the median UIC is below 100.0μg/L. In addition, less than 20% of the urine samples should have UIC below 50.0μg/L. The median UIC can also be used to indicate the severity of iodine deficiency; for example, a population with median UIC below 20.0μg/L is considered severely deficient; moderately or mildly deficient if median UIC is 20.0 to 49.0μg/L or 50.0 to 99.0μg/L respectively [1].

A total of 190 survey questionnaires were randomly distributed among members in the Zia community. The completed questionnaires were collected and transported to the MRL SMHS UPNG for analysis. The questionnaires were coded and the data entered into an Excel database. The data was analysed using SPSS software (version 21 for Windows).

Ethical approval: Ethical approval was obtained from the Ethics and Research Grant committee in SMHS UPNG and the PNG National Department of Health Medical Research Advisory Committee (NDoH MRAC). In additions, verbal consent was obtained from village authorities, and each adult participant and primary caretaker of the children. The consent of each of the participants was documented on the respective interview form. This consent procedure was approved by the ethics committees.

RESULTS:

Availability of salt in households:

To assess the availability of salt in the households, a total of 163 children were each given a zip locked bag and asked to bring a spoon of the salt from their household. A total of 159 zip-lock bags with salt were retuned. This indicates that salt was available in 97.5% (159/163) of the households.

Assessment of Iodine content in salt from Households and trade stores:

The summary statistics of the Iodine content in the salt samples from the households are presented in Table 1. The mean (± STD) Iodine content was 31.7 ± 5.9mg/kg (ppm), range was 8.3 – 43.5 mg/kg. The distribution of the iodine content in salt samples from households based on the criteria in the PNG salt Legislation, shows that iodine content was inadequate (5.0 – 29.9 mg/kg) in 37.1% (59/159) of the salt samples and adequate (30.0 – 50.0 mg/kg) in 62.9% (100/159). Using the criteria recommended by the WHO/IGN/IGN [3, 4], 98.7% (157/159) of the households had salt with iodine content above the 15.0mg/kg for adequately iodized salt. This is above the 90.0% recommended coverage for households with adequately iodized salt that should indicate effective implementation of the USI strategy [3, 4]. The mean iodine content in the three brands of salt from the trade stores were 35.5mg/kg, 37.5mg/kg and 25.7mg/kg respectively.

Table 1: Summary statistics of the Iodine content in mg/kg (ppm) in salt from households in Zia community

Parameters	Iodine content (mg/kg)
Mean	31.7 mg/kg
Standard Deviation (STD)	5.9
95% Confidence Interval (95% CI)	30.8 – 32.6 mg/kg
Range	8.3 – 43.5 mg/kg
Median	32.3 mg/kg
Interquartile range (IQR)	27.4 – 36.2 mg/kg

Assessment of discretionary intake of salt in households:

The assessment of discretionary intake of salt was conducted by providing a pre-weighed (250g) package of iodised salt to the heads of 40 randomly selected households to use for food preparation and consumption as usual. During the first visit, consent was obtained from the head of the household and the total number of individuals in the household was recorded. Each household was revisited three days later. The salt remaining in the package was reweighed to the nearest 0.1g and the total number of individuals in the household was rechecked. The

total amount of salt consumed was calculated and used to determine the per capita discretionary intake of salt per day. The frequency distribution of the discretionary intake (g) of salt per capita per day in the various households shows that among the 40 households 25.0% (10/40) were consuming between 2.0 to 5.0 g of salt per capita per day and 75.0% (30/40) were consuming between 6.0 to 10.0 g of salt per capita per day. The summary statistics of the discretionary intake of salt per capita per day is presented in Table 2. The mean per capita discretionary intake of salt was 5.7 ± 2.2 g/day and the range was 1.7 to 10.0 g/day.

Table 2: Summary statistics of the per capita discretionary intake (g) of salt per day in households in Zia community

No (number of households)	40
Mean	5.7 g/day
Standard deviation (STD)	2.2
95% Confidence Interval (95% CI)	5.0 – 6.5 g/day
Range	1.7 – 10.0 g/day
Median	5.4 g/day
Interquartile range (IQR)	4.3 – 7.7 g/day

Mean per capita discretionary intake of iodine per day in households in Zia:

In the households the mean discretionary intake of salt per capita per day was 5.7 $\pm$ 2.2g and the mean iodine content in the salt was 31.7mg/kg. Thus, the calculated mean discretionary intake of iodine per capita per day was 180.7 $\pm$ 69.7µg, with a range of 53.9 to 317.0µg per capita per day.

Assuming that 30% of the iodine in salt was lost during storage and food preparation, the calculated per capita discretionary intake of iodine becomes 126.5 ± 48.8µg per day, with a range of 37.7 to 221.9µg per day. Thus, the calculated mean discretionary daily per capita intake of iodine is within the 90.0µg to 120.0µg recommended daily requirement of iodine for children, but below the 150 to 200µg recommended for non-pregnant, pregnant and lactating women in the households [1, 3, 4].

Anthropometry**:**

A total of 388 children age 6 to 12 years selected from 5 schools in the Zia community Huon district participated in this study. The anthropometric parameters of all the children are presented in Table 3. Their mean weight was 25.1 ± 6.5 kg and the range was 13.2 to 56.9 kg. Their mean height was 126.9 ± 11.6 cm and the range was 90.5 to 160.0 cm.

Table 3: Anthropometric parameters of all the children and of the male and female children

	All children (n = 388)		Males (n = 227)		Females (n = 161)	
	Weight (kg)	Height (cm)	Weight (kg)	Height (cm)	Weight (kg)	Height (cm)
Mean	25.1	126.9	24.8	126.3	24.5	127.7
Std Dev	6.5	11.6	5.8	11.2	7.4	12.2
95% CI	24.4 – 25.7	125.7 – 128.0	24.0 – 25.6	124.8 – 127.7	24.3 – 26.6	125.8 – 129.6
Range	13.2 – 56.9	90.5 – 160.0	13.2 – 46.7	90.5 – 156.0	13.3 – 56.9	102.0 – 160.0
Median	24.3	126.5	24.3	126.0	24.2	127.5

The 388 children were separated according to their gender; 58.5% (227/388) of the children were male and 41.5% (161/388) were female. The mean weight of the male children was 24.8 ± 5.8kg and the mean height was 126.3 ± 11.2cm. For the female children the mean weight was 24.5 ± 7.4kg and the mean height was 127.7 ± 12.2 cm (Table 3). There was no statistically significant difference between the weight of the male and female children, and also between the height of the male and female children.

Urinary Iodine Concentration (UIC):

To assess the Iodine status of the school children in the community, a total of 388 children were randomly selected from 5 primary schools. Casual urine samples were collected from 381 children after obtaining informed consent from their parents. This gave a consent rate of 98.2% (381/388).

The Kolmogorov-Smirnov test (p = 0.001) for normality confirms that the UIC (µg/L) for the children was not normally distributed. Thus, non-parametric statistics were used for analysis of the UIC data. The summary statistics of the UIC (µg/L) are presented in Table 4. The Median UIC for all the children was 147.5µg/L and the Interquartile Range (IQR) was 110.4 – 215.0µg/L. In addition, 3.7% had UIC below 50.0µg/L. The results indicate normal status of iodine nutrition at the time of this study.

Table 4: Summary statistics of Urinary Iodine Concentration (µg/L) for all the children and for the male and female children

	All children (n =381)	Male children (n = 221)	Female children (n = 160)
Median UIC (µg/L)	147.5	153.4	141.2

Interquartile Range (IQR) (µg/L)	110.4 – 215.0	111.7 – 217.7	103.3 – 206.8
95% Confidence interval (Bootstrapping) (µg/L)	138.2 – 157.2	143.1 – 166.7	129.4 – 154.4
Percent (n) of children with UIC below 50µg/L	3.7 (14)	3.6 (8)	3.8 (6)

The UIC data for the children were separated according to gender; 58.0% (221/381) were male and 42.0% (160/381) were female children. The summary statistics of the UIC (µg/L) for the male and female children are presented in Table 4. Using the Mann-Whitney U and Wilcoxon W tests, no statistically significant difference (p = 0.751, 2-tailed) was observed between the UIC for the male and female children.

Goiter rate**:**

Goiter was palpable (grade 1) on 44.5% (169/380) of the children, but not palpable (grade 0) on 55.5% (211/380). Urine samples were collected from 380 (97.9%) of the 388 children. The summary statistics of the UIC for children with palpable and non-palpable goiter are presented in Table 5.

The median UIC for the children with palpable goiter was 156.40µg/L and the IQR was 109 – 229µg/L. For the children with non-palpable goiter the median UIC was 145.6µg/L and the IQR was 111 – 209µg/L. There was no statistically significant difference in the UIC for children with palpable goiter compared to those with non-palpable goiter (p = 0.67, 2-tailed).

The results for goiter were further analyzed according to gender. Table 5 shows the number of male and female children with palpable and non-palpable goiter. The summary statistics of the UIC for the male and female children are also presented in Table 5. There were no statistically significant differences between the male and female children with and without palpable goiter.

Table 5: Summary statistics of UIC of all the children and for the male and female children with palpable and non-palpable goiter

	All children (n = 380)		Male children (n = 220)		Female children (n = 160)	
	Palpable goiter	Goiter not palpable	Palpable goiter	Goiter not palpable	Palpable goiter	Goiter not palpable
Percent (n)	44.5% (169)	55.5%(211)	38.6% (85)	61.4% (135)	52.5% (84)	47.5% (76)
Median (µg/L)	156.4	145.6	163.4	149.4	143.5	139.9

IQR (μg/L)	109 – 229	111 – 209	117 – 235	111 – 216	103 – 217	109 – 188
Bootstrapping (95% CI) μg/L	163 – 194	151 – 172	160 – 205	151 – 182	148 – 190	139 – 172
% (n) with UIC below 50μg/L	4.7% (8)	2.8% (6)	5.9% (5)	2.2% (3)	3.6% (3)	3.9% (3)

Assessing the availability and awareness of Iodised Salt, use of Salty Condiments, Flavourings, and Fortification Food Vehicles in the Zia community:

Of the 190 questionnaires distributed, 180 were collected. A total of 172 questionnaires were found suitable for analysis. This gave a response rate of 90.5% (172/190). Both English and Tok-Pisin versions of the questionnaire were presented to each of the respondents with a request to select the one that was appropriate for them to complete. Assistance was provided to those who requested help in completing the questionnaires.

Socio-demographic characteristics of the respondents:

The socio-demographic characteristics of the respondents are presented in Table 6. The mean age of all the respondents was 31.8 ± 14.5 years, age range 15.0 to 93.0 years. Gender distribution of the respondents shows that 41.3% (71/172) were females and 58.7% (101/172) were males. For further presentation of the results, the data was not be separated according to gender.

Of the 172 respondents 53 (30.8%) had no formal education, 94 (54.6%) had primary education, 24 (14.0%) had secondary education and only 1 (0.6%) completed university. At the time of this study, the university graduate was on holidays in the village. It is important to note that low education level and remoteness may contribute to apparent lack of awareness of the importance of iodised salt in a community. For their marital status, 60.3% (102/169) of the respondents were married.

The respondents were asked if they had a salaried job. Of the 168 that answered this question, 87.5% (147/168) said that they do not have a job with salary. This is because most of them are either fishermen or subsistence farmers. They do not consider the amount of money that they receive after selling their products as salary.

TABLE 6: Socio-Demographic Characteristics of Respondents		
1.	Gender (N = 172)	
	Females	41.3% (71/172)
	Males	58.7% (101/172)

2.	Age (years) of participants	
	Mean age of females (years) (N =71)	29.3 ± 14.5
	Mean age of males (years) (N = 101)	33.6 ± 14.5
	Mean age of respondents (years) (N = 172)	31.8 ± 14.5
	Age range of respondents (years)	15.0 – 93.0
3.	Education level (N = 172)	
	Primary	54.6% (94)
	Secondary	14.0% (24)
	University	0.6% (1)
	None	30.8% (53)
4.	Marital status (N = 169)	
	Single	34.9% (59)
	Married	60.3% (102)
	Separated / Divorced	1.8% (3)
	Widow / Widower	3.0% (5)
5.	Do you have a job with a salary (pay)? (N = 168)	
	Yes	12.5% (21)
	No	87.5% (147)

Availability and Awareness of Iodized Salt and use of Salty Condiments, Flavourings, and Fortification Food Vehicles**:**

The questionnaire contains 21 questions. The results obtained are presented in Table 7. In response to the first question (Q1) "*Does your household use anything to give food a salty taste?*" The response by 96.5% (164/170) of the respondents was in the affirmative.

The second question (Q2) was to select from a list provided the products used in the household (HH) to give food a salty taste. Salt bought from the markets or shops was selected by 90.9% (149/164) of the respondents; Maggi Kakaruk stock cube was the next product selected by 93.9% (154/164) of respondents, followed by Super Chicken stock cubes by 45.7% (75/164) of the respondents.

When asked (Q3), how often products other than salt bought at the market and shop were used in their HH, respondents stated that Maggi Kakaruk stock cube was used more frequently, compared to the other products; 50.6% (78/154) used Maggi Kakaruk every day, 41.6% (64/154) used it several times a week. The results showing frequency of use of the other products are presented in Table 7.

In order to assess the availability of salt in the HH, the 149 respondents that use salt were asked (Q4) *"Does your family have salt bought at market/shop in the household today?"* A total

of 95.3% (142/149) of the respondents answered in the affirmative. The next question (Q5) was for those that answered negative to Q4. Of the 7 respondents 5 (71.4%) answered in the affirmative. Those that answered negative to Q5 were asked Q6. One of the two respondents asked Q6 answered in the affirmative, that the HH has salt "bought in the market/ shop any day in the last 7 days". The result, however, indicates that majority of the respondents had some amount of salt in the HH on any day in the preceding seven days.

In response to the question (Q7), if iodised salt was available in the local market/shop where food is commonly purchased, 93.9% (123/131) said "Yes". Respondents that use salt were asked (Q8) "*What do you do with the salt bought at market/shop?*" Four options were provided; *they were asked to select as many as possible*. In response, 81.2% (121/149) stated that they use salt for cooking and add it to food before eating; 30.9% (46/149) use salt for cooking only; 16.1% (24/149) add salt to food before eating only and 49.7% (74/149) of the respondents stated that they also have other uses for salt. They did not specify as requested in the questionnaire, but verbally stated that they use salt for preparation of herbal remedies and preparation of chicken feeds.

The respondents were asked (Q9) "*Why do you buy salt at market/shop only once a month or less?"* 2.7% (4/149) said that salt was too expensive, 32.9% (49/149) said salt was not always available, 40.9% (61/149) said that they do not like salt and 23.5% (35/149) prefer to use other products to make food salty. The respondents were then asked (Q10) "*If iodised salt was easily available at market/ shop and was affordable, would your household buy it?*" The answer was "Yes" by 90.9% (149/164) of the respondents.

In order to assess the awareness and knowledge about the importance of iodised salt, the respondents were asked (Q11) *"Do you think there are health benefits using iodised salt bought from market/shop?* Of the 152 respondents that answered the question, 40.1% (61) said "Yes" and 52.6% (80) said that they were not sure.

To obtain information about commonly available commercial foods that can be fortified the respondents were asked (Q12) "*Does your household have wheat flour or wheat flour foods such as dried noodles, pasta, macaroni, instant noodles; 2-minute noodles, bread, buns, rolls, cake, crackers, biscuits, scones, donuts today?*" Only 32.3% (53/164) of respondents said "Yes". The next question (Q13) to the 111 respondents that answered in the negative was "*If No, did your household have wheat flour or wheat flour foods, such as, dried noodles, pasta, macaroni, instant noodles, 2-minute noodles, bread, buns, rolls, cake, crackers, biscuits, scones, donuts yesterday?*" a total of 38.7% (43/111) said "Yes", compared to 61.3% (68/111) that said "No". The

follow up question (Q14) was to the 68 respondents that answered in the "negative". Of the 68 respondents, 44 (64.7%) said "Yes". This indicates that these products were available in the HH of a relatively large number of the respondents in the last seven days.

In the next question (Q15) those participants that had responded "Yes" to the questions on wheat (Q12, Q13 and Q14) were asked which wheat products they had in their HH, and that they could choose as many as necessary from the options given. A total of 140 respondents answered Q15. The result is presented in Table 7. In summary, 85.0% (119/140) of the respondents selected "Instant noodles/2-minute noodles" as the most popular wheat product in their HH. Both "Crackers/biscuits" and "Wheat flour" were the next products selected by 22.1% (31/140) of the respondents.

The next set of questions (Q16, Q17, and Q18) was on the availability of rice in the HH. In response to Q16, a total of 52.9% (90/170) of respondents did not have rice in the HH on the day of the visit. In response to Q17, 51.1% (46/90) did not have rice in the HH the previous day, and in response to Q18, 56.5% (26/46) said they did not have rice in the HH any day in the last seven days.

Respondents were also asked (Q19, Q20, and Q21) about the availability of oil in their HH. On the day of the visit, 59.4% (101/170) did not have oil in their HH. In response to the next question Q20, if they had oil in the HH the previous day, 65.3% (66/101) responded in the negative. They were then asked if they had oil in the HH any day in the last seven days; 54.5% (36/66) also responded in the negative.

Table 7: Summary of answers on availability and awareness of iodised salt, and use of salty condiments, flavourings, and fortification food vehicles

Q1	Does your household use anything to give food a salty taste? (N = 170)	% (N)
	1. Yes	96.5% (164)
	2. No	3.5% (6)
	3. Not sure	0
Q2	If yes, what do you use? Select as many as apply (N = 164) (some participants selected more than one product)	
	1. Salt bought at market / shop:	90.9% (149)
	2. Maggi Kakaruk stock cubes	93.9% (154)
	3. Super chicken stock cubes:	45.7% (75)
	4. Soya/ Maggi sauce	32.9% (54)
	5. Kakaruk salt:	19.5% (32)
	6. Other seasoning:	13.4% (22)

	7. Ash/traditional salt:	3.7% (6)
	8. Salty water from river/sea	25.6% (42)
Q3	How often do you use the products (other than salt bought at the market /shop) mentioned in question 2? (Give details for the first 3 products)	
	Maggie Kakaruk stock cubes (n = 154):	
	1. Everyday	50.6% (78)
	2. Several times a week	41.6% (64)
	3. Once a week	4.5% (7)
	4. Once a month or less	3.2% (5)
	Super chicken stock cubes (n = 75):	
	1. Everyday	37.3% (28)
	2. Several times a week	46.7% (35)
	3. Once a week	10.7% (8)
	4. Once a month or less	5.3% (4)
	Soy / Maggie sauce (n = 54):	
	1. Everyday	22.2% (12)
	2. Several times a week	44.4% (24)
	3. Once a week	18.5% (10)
	4. Once a month or less	14.8% (8)
Q4	Does your family have salt bought at market / shop in the household today? (N = 149)	
	1. Yes	95.3% (142)
	2. No	4.7% (7)
Q5	If no, did your household have salt bought at market / shop yesterday? (N = 7)	
	1. Yes	71.4% (5)
	2. No	28.6% (2)
Q6	If no, did your household have salt bought at market / shop any day in the last 7 days? (N = 2)	
	1. Yes	50% (1)
	2. No	50% (1)
Q7	Is iodised salt available in the local market / shop where food is commonly purchased? (N = 131)	
	1. Yes	93.9% (123)
	2. No	3.1% (4)
	9. Not sure	3.0% (4)
Q8	What do you do with the salt bought at market / shop? Select as many as possible (N =149) (More than one option was selected; total does not add up to 100%)	
	1. Use for cooking and add to food before eating	81.2% (121)
	2. Use for cooking only	30.9% (46)
	3. Add to food before eating only	16.1% (24)
	4. Other uses (Specify)	49.7% (74)
Q9	Why do you buy salt at market / shop once a month or less? (N = 149)	
	1. Too expensive	2.7% (4)
	2. Not always available	32.9% (49)
	3. Do not like it	40.9% (61)
	4. Prefer to use other products to make food salty	23.5% (35)

Q10	If iodised salt was easily available at market / shop and was affordable, would your household buy it? (N = 164)	
	1. Yes	90.9% (149)
	2. No	7.3% (12)
	9. Not sure	1.8% (3)
Q11	Do you think there are health benefits using iodised salt? (N = 152)	
	1. Yes	40.1% (61)
	2. No	7.2% (11)
	9. Not sure	52.6% (80)
Q12	Does your household have wheat flour or wheat flour foods such as dried noodles, pasta, macaroni, instant noodles; 2-minute noodles, bread, buns, rolls, cake, crackers, biscuits, scones, donuts today? (N = 164)	
	1. Yes	32.3% (53)
	2. No	67.7% (111)
Q13	If no, did your household have wheat flour or wheat flour foods such dried noodles, pasta, macaroni, instant noodles, 2-minute noodles, bread, buns, rolls, cake, crackers, biscuits, scones, donuts yesterday? (N = 111)	
	1. Yes	38.7% (43)
	2. No	61.3% (68)
Q14	If no, did your household have wheat flour or wheat flour foods such as dried noodles, pasta, macaroni, instant noodles, 2-minute noodles, bread, buns, rolls, cake, crackers, biscuits, scones, donuts on any day in last 7 days? (N = 68)	
	1. Yes	64.7% (44)
	2. No	35.3% (24)
Q15	If you responded “Yes” to question 12, 13, or 14, which food did you have in your household (tick all that you have)? (N = 140) (Some selected more than one thus, the total does not add up to 100%)	
	1. wheat flour	22.1% (31)
	2. dried noodles/macaroni/pasta	16.4% (23)
	3. Instant noodles/2-minute noodles	85.0% (119)
	4. Bread/buns/rolls/	5.7% (8)
	5. Crackers/biscuits	22.1% (31)
	6. Cake/scones/donuts	12.1% (17)
Q16.	Does your household have rice today? (N = 170)	
	1. Yes	47.1% (80)
	2. No	52.9% (90)
Q17.	If no, did your household have rice yesterday? (N = 90)	
	1. Yes	48.9% (44)
	2. No	51.1% (46)
Q18.	If no, did your household have rice any day in the last 7 days? (N = 46)	
	1. Yes	43.5% (20)
	2. No	56.5% (26)
Q19.	Does your household have oil today? (N = 170)	
	1. Yes	40.6% (69)
	2. No	59.4% (101)
Q 20.	If no, did your household have oil yesterday? (N = 101)	
	1. Yes	34.7% (35)

	2. No	65.3% (66)
Q 21.	If no, did your household have oil any day in the last 7 days? (N = 66)	
	1. Yes	45.5% (30)
	2. No	54.5.% (36)

DISCUSSION:

Effective implementation and monitoring of the USI is the most equitable and sustainable strategy to ensure optimal iodine nutrition for all population groups [3]. It is the main strategy for achieving sustained IDD control among all groups in the urban, rural and remote communities worldwide. Thus, the need to ensure adequate iodization of all food grade salt cannot be overemphasized. Quantitative assessment of the iodine content in salt is one of three parameters that can be used for assessing the iodine status in a population [1, 3]. It is the most important "Process" indicator for monitoring progress in the implementation of the USI, which is one of the most effective and sustainable long-term public health measures for the prevention and control of iodine deficiency [1, 2, 3].

In this project, the PNG salt legislation [7, 8] was used to evaluate the iodine content in salt available in the households. The daily per capita discretionary intake of salt was 5.7 $\pm$ 2.2g. This value is lower than the recommended 10.0g per capita per day salt intake stipulated in PNG salt legislation [7, 8]. It is also lower that the 6.59g per capita per day intake in Lae City Morobe province [19] and the 6.0g reported for households in Sina-Sina Yonggomugl in Simbu [14]. However, it is higher than the 2.62g per capita per day salt consumption in Hela region [10], the 4.7g and 4.6g per capita per day reported in Eastern Highlands and Karimui-Nomane in Simbu provinces [11].

Of the 163 households selected in the present study, no salt was available in 4 (2.5%) of the households; in addition, the iodine content in only two (1.3%) of the households with salt was below 15mg/kg. Thus, according to the WHO/UNICEF/IGN criteria [1, 3], 97.5% (159/163) households had adequately iodized salt at the time of this study. This is above the 90.0% recommended coverage of households with adequately iodized salt that should indicate effective implementation of the USI strategy.

However, according to the PNG Salt Legislation, of the 159 households with salt, the iodine content in 59 (37.1%) salt samples was below the 30.0 mg/kg cut-off point recommended in the PNG salt legislation [7, 8]. Salt with iodine content above 30.0ppm was available in 62.9% (100/159) of the households. Thus, 62.9% of randomly selected households in the Zia community had adequately iodized salt at the time of this study. This value is lower than the

90.0% coverage of households with adequately iodized salt that should indicate effective implementation of the PNG Salt legislation. This should be of concern to program planners in the National Department of Health (NDOH) and the Morobe provincial authorities, because of the severe consequences of iodine deficiency in young children, pregnant and lactating mothers, and also because of the devastating effect of iodine deficiency on the developing brains of neonates [1, 2, 3].

Two of the three brands of salt from the trade stores were adequately iodized. The low iodine content in the salt samples from the 37.1% of households might be due to several factors relating to poor storage and handling of the salt in these households. Further study is need to ascertain the factors that could result in loss of iodine in salt in the households.

The calculated mean per capita discretionary intake of iodine was 180.7µg ± 69.7µg/L. This was higher than the 90µg to 120µg daily intake of iodine recommended for children [1]. Assuming that the iodised salt is added directly to the ready-to-eat food, then this is just within the 150µg to 200µg recommended daily requirement of iodine for adults, including pregnant and lactating women [1, 2, 3]. If, however, the iodised salt is added during food preparation, then, factoring in the about 30% loss of iodine in salt during storage and food preparation, the calculated per capita discretionary intake of iodine becomes 126.5µg. This amount is lower than the recommended daily requirement for non-pregnant, pregnant and lactating women [1, 2, 3]. This indicates the need to carry out intensive education and awareness campaigns in the community, advocating the use of iodized salt (when it is available and affordable).

In the present study, the status of iodine nutrition among the children was assessed using the current WHO/UNICEF/IGN recommended epidemiological criteria and the recommended indicators for assessing and monitoring progress towards the elimination of iodine deficiency as a Public Health problem in affected communities [1, 3]. According to the criteria, optimal status of iodine nutrition is achieved when the median UIC in the population is 100 – 200µg/L. The UIC does not usually exceed the dietary intake of iodine; it is therefore possible to use the UIC as a biochemical parameter for assessing the iodine status of a population [1, 3]. The median UIC (µg/L) in a population is the Prime Biochemical Index for evaluating the degree of Iodine Insufficiency in a target population.

School children in the 6 – 12 years age group are recommended for the assessment of iodine nutrition in a population because of their high vulnerability to iodine deficiency and easy accessibility in the community [1]. The school-

based approach was used in this study because of the supposedly high enrolments and attendance of both male and female children in primary schools in Huon district.

A total of 388 children were selected randomly from 5 schools. The response rate of 98.2% (381/388) obtained in the present study was higher than the 90.0% predicted response rate used for the determination of the sample size.

The median UIC for all the children was 147.5µg/L and the UIC was below 50.0µg/L among 3.7% (14/381) of the children. This indicates normal status of Iodine nutrition at the time of this study. Thus, Iodine deficiency should not be considered as a significant public health problem among schoolchildren, age 6 – 12 years in the Zia community in Huon districts at the time of this study.

The median UIC value for all the children was higher than the value reported for schoolchildren aged 6 – 12 years in Southern Highlands province, PNG (48.0ug/L) [10], Simbu province (17.5µg/L and 58.5µg/L), Gulf and other remote areas in PNG [14, 16, 20], but lower than the value reported in Keita District Bougainville in PNG (204.5µg/L), Honduras (287ug/L) [21], Nicaragua (259ug/L), El Salvador (251ug/L), Chile (565ug/L), Ecuador (590ug/L), Brazil (1013ug/L) and Mexico (1150ug/L) [22].

Normal status of iodine nutrition was also prevalent among the male and female children with median UIC of 153.4µg/L and 141.2µg/L, respectively. The data shows that, based on the median UIC, the Iodine nutrition status in the Zia community in Huon district should not be considered critical among the male and female children in the 6 to 12 years age group, at the time of this study.

Contrary to the results obtained for the median UIC in the present study, a total of 44.5% of all the children had palpable goiter (grade 1). This indicates long-standing prevalence of mild status of iodine deficiency among the children [1].

Discrepancies between the results for UIC and prevalence of goitre:

Despite the normal status of iodine nutrition based on the median UIC obtained in the present study, 44.5% (169/380) of the children had palpable goitre, which may indicate mild prevalence of iodine deficiency. This discrepancy may be explained by the fact that median UIC reflects the current situation of iodine supply, while thyroid size indicates the long-term iodine status [1, 23].

The prevalence of iodine deficiency determined by the two indicators does not necessarily need to be consistent [23]. The median UIC also

indicated adequate intake of iodine at the time of the study.

Another explanation for the discrepancy may be because of the inadvertent error made during the pre-visit to the community to obtain permission before the collection of urine samples. The pre-visit was carried out about five days before commencement of sample collection. Several packets of iodised salt were distributed to the community leaders during the pre-visit. This might have resulted in the high number of households with iodised salt and the high rate of consumption of iodised salt in the households. The donation of the salt packages is one of the traditional ways of obtaining the approval for the project to proceed with full cooperation of the community. Thus, the need for further studies to be carried out to corroborate the results obtained in the present study.

Questionnaire:

More males (58.7%) than females (41.3%) completed the questionnaires. All the respondents were adults with mean age of 31.8 years. The level of education in the community was low, as only 14.6% had attained education above primary school level. Remoteness and low level of education are factors that can contribute to an apparent lack of awareness of the need to consume adequate amounts of iodine for optimal growth and development [1]. This might be one of the reasons for the 44.5% of children with palpable goitre in the present study. According to a recent study, low socioeconomic status and rural residence were found to be risk factors for low household access to salt [24]. In the present study, the donation of adequately iodised salt packages to the community leaders as incentive for participation in the study may have skewed the results.

Majority of the households (93.9%) used Maggi Kakaruk stock cubes to make their food salty, compared to 90.9% that used salt. Among those households that used Maggi Kakaruk cubes, 50.6% use them every day and 41.6% use them several times a week. The results also show that both Maggi Kakaruk cubes and salt are used in most of the households, when they are available and affordable.

The need for advocacy and increased awareness to educate the people about the health benefits of using iodised salt cannot be overemphasized. This is because only 40.1% of the respondents were aware of the health benefits of using iodised salt. Most of them said that they became aware after the presentation made to them during the pre-visit.

On the day of the visit, 85.0% of respondents had Instant noodles/2-minute noodles available in the households compared to 22.1% of households with wheat flour. This strongly suggests that instant noodles/2-minute noodles

are the best wheat based alternative processed foods that should be fortified with iodine. This can be achieved by preparing these wheat-based products with adequately iodised salt.

The consumption of rice (47.1%) and oil (40.6%) can be considered as moderate. However, rice was available in 84.7% (144/170) of households at least once in the last seven days. Similarly, oil was available in 78.8% (134/170) of households at least once in the last seven days.

However, salt and Maggi Kakaruk stock cubes are the two optimal food vehicles for fortification with iodine in this remote community.

CONCLUSIONS:

Salt with iodine content above 30.0ppm was available in 62.9% of the households. The low coverage of households with adequately iodized salt at the time of this study indicates poor implementation of the PNG Food Sanitation Regulation. The daily per capita discretionary intake of salt was 5.7g. The calculated per capita discretionary intake of iodine was 126.5µg per day. The median UIC among the children indicates normal iodine status at the time of this study. Contrary to the results obtained for the median UIC, a total of 44.5% of all the children had palpable goiter (grade 1). This may indicate long-standing prevalence of mild status of iodine deficiency. Majority of the households (93.9%) used Maggi Kakaruk stock cubes to make their food salty, compared to 90.9% that used salt. Instant noodles/2-minute noodles are the best wheat based alternative processed food that should be fortified with iodine. Salt and Maggi Kakaruk stock cubes are the two optimal food vehicles for fortification with iodine in this remote community.

Limitations of the study:

One of the major limitations of this study was the way the community elders' cooperation was obtained. Traditionally, the elders' approval for research in some remote communities is secured by providing appropriate incentives to the community leaders for distribution to members of the community. In the present study, several packets of iodised salt were donated to the community leaders in order to obtain their approval for community participation. This may have skewed the results in favor of the high number of households with iodised salt and the high rate of consumption of iodised salt in the households. Thus, more studies should be carried out to corroborate the results obtained in the present study.

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ASSESSMENT OF THE ASSOCIATION BETWEEN RAINFALL AND CLIMATE-SENSITIVE INFECTIONS USING SYNDROMIC SURVEILLANCE SYSTEMS: A LITERATURE REVIEW WITH IMPLICATIONS FOR SYNDROMIC SURVEILLANCE IN PACIFIC ISLAND COUNTRIES

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ABSTRACT:
Although Pacific Island countries are vulnerable to the effects of climate change, studies evaluating climate change's influence on infectious disease trends within the region are scanty. A rapid literature review was conducted to assess available published information on the association between infectious disease syndromes and rainfall. This paper discusses the review findings that have important implications for syndromic surveillance of climate-sensitive infections in Pacific Island countries. Google Scholar and PubMed were used to find literature assessing the association between infectious disease syndromes and rainfall. The purpose of the rapid review was to provide background information for a study aimed at determining whether the trends of infections are associated with rainfall in Pohnpei. The results showed influenza-like illnesses may be positively correlated with rainfall, but the trends are also determined by seasonal presence of respiratory viruses. Diarrhoeal diseases are influenced by both heavy rainfall and drought. Febrile illnesses are associated with rainfall through the effect of rainfall on disease vectors. Weather factors may influence COVID-19 transmission, but current literature is inconclusive. Association between infectious disease trends and rainfall is multifactorial and geography-specific. Conclusions from studies in one geographical region cannot be applied globally, and further research is needed in the Pacific to examine this phenomenon locally.

Keywords: climate change, climate-sensitive infections, syndromic surveillance, mosquito-borne infections, Pacific island countries.

INTRODUCTION:

Recently, considerable literature has grown around climate-sensitive infections, specifically the association with weather variables. For example, diarrhoea and febrile illnesses are linked to heavy rain or drought [1]. At the same time, influenza-like illnesses (ILI) are associated with cold temperatures [2,3]. Surprisingly, similar studies evaluating the association between infectious disease syndromes and weather within the Pacific region are scanty,

even though this region is vulnerable to the effects of climate change.

Leptospirosis, diarrhoea, and respiratory illnesses are potential climate-sensitive infections in the Federated States of Micronesia (FSM) [4]. McIver et al. [4] suggested that these infections may be linked to the rainfall pattern, similar to studies elsewhere [5-7]. Furthermore, McIver et al. [4] identified knowledge gaps in the data for these climate-sensitive infections across the four states of FSM. The authors suggested that gaps in their data could be due to unreliable health information systems or human skills capacity constraints. Hence, the authors concluded that the amount of data available for their assessment was inadequate, and no further analysis could be done. They recommended increased research on the epidemiology of climate-sensitive infectious diseases in FSM to provide accurate data on the association between climate-sensitive infections and rainfall patterns [4].

The Pohnpei State Hospital implemented an electronic health record (EHR) system in 2019. The improvement in the hospital's health information system was an initiative of the national FSM government. This literature review guided a research project to assess the association between rainfall and infectious disease syndromes using data generated by the electronic health information system at the Pohnpei State Hospital.

The following questions directed this literature review:

(1) What is the association between rainfall and diarrheal illnesses?

(2) What is the association between rainfall and influenza-like illnesses (ILI), including coronavirus disease 2019 (COVID-19)?

(3) What is the association between rainfall and febrile illnesses?

(4) What is the association between rainfall and leptospirosis? This review focused on studies conducted in the Asia Pacific Region, with particular attention to studies done in the FSM and other small Pacific Island countries. Relevant studies done outside the Asia Pacific Region but with direct implications for Pacific Island countries were also included.

METHODOLOGY:

Google Scholar and PubMed were searched for relevant literature. The keywords used were syndromic surveillance, infectious disease outbreak, Pacific, disease surveillance, infectious disease surveillance, climate change and syndromic surveillance trend.

Boolean operators AND, OR were used as conjunctions to combine the keywords in varying combinations and arrangements to maximise search output [8]. This strategy was repeated with all keywords until all valid combinations were exhausted. Exhaustion of keyword combinations and arrangements was reached when Google Scholar or PubMed search results

contained the same articles as previous searches.

The abstracts of all papers were screened using pre-defined inclusion and exclusion criteria. All search results from PubMed were included for initial screening, but only the first ten results from Google Scholar were scanned for relevant articles. All literature was managed using Zotero software.

Article inclusion criteria were defined as (1) peer-reviewed open access quantitative and qualitative literature, (2) government or non-government reports, (3) consensus statements, (4) conference proceedings and (5) studies conducted in the Asia-Pacific region.

Exclusion criteria were (1) studies conducted outside the Asia-Pacific region except studies that has direct link to the Pacific region, (2) non-English publications, (3) opinions except editorials and (4) personal web pages. Duplicate articles were deleted.

Data were extracted using the following themes: (1) rain events and ILI, including COVID-19, (2) rain events and febrile illnesses, (3) rain events and diarrhoea and (4) rain events and leptospirosis. A separate theme for rain events and leptospirosis was used for data extraction because it is the most severe vector-borne infection associated with rain in Pohnpei. Other vector-borne febrile illnesses such as malaria, dengue and other viral mosquito-transmitted infections are not endemic in Pohnpei.

RESULTS:

The initial search identified 94 articles. The abstracts were then reviewed using the inclusion and exclusion criteria. Finally, 43 articles were selected for in-depth reading and data extraction.

Extracted data were summarised under the following headings: (1) Definition of syndromic surveillance, (2) Syndromic surveillance in Pacific Island countries, (3) Association between rainfall and diarrhoeal illnesses, (4) Association between rainfall and febrile illnesses, (5) Association between rainfall and influenza-like-illnesses, and (6) Association between weather and COVID-19.

Definition of syndromic surveillance:

Syndromic surveillance systems vary depending on the point of data collection and objective. For example, event-based syndromic surveillance is used in mass gatherings, while electronic methods detect infectious disease outbreaks using routine clinical data from outpatient or emergency departments [9]. Syndromic surveillance systems are, therefore, highly adaptable and suitable for rapid deployment. These characteristics of syndromic surveillance systems have allowed this form of public health surveillance to serve many needs.

The advantages and disadvantages of a syndromic surveillance system depend on the type of surveillance used. For example, event-based surveillance is deployable rapidly but is

labour intensive and not scalable [9]. Electronic surveillance systems allow them to be scalable, data is standardised, and data mining can be done but have the disadvantage of being potentially expensive [9].

Syndromic surveillance systems are disease-focused and automated, but the systems' sensitivity to detect syndromes depends on many factors. Specifically, the nature of case definitions used in describing syndromes in syndromic surveillance systems affects the sensitivity and positive predictive value of the case definitions or syndrome definitions. For example, a study by Guasticchi et al. [10] showed 90% sensitivity for coma but only 22% for hemorrhagic diarrhoea. In the same study, the positive predictive value of syndromes ranged between 99.3% and 20% [10]. The sensitivity of syndromic surveillance to detect waterborne outbreaks is also highly variable and depends on multiple environmental and other health factors [11]. Therefore, syndromic surveillance systems have the potential to detect a lot of false signals. This apparent disadvantage is offset by system automation enabling faster response because a delay can be costly both in material terms and in lives lost, particularly in low-resource settings. Furthermore, emergency departments using syndromic surveillance for COVID-19 surveillance have shown that having a syndromic surveillance system that detects a lot of false positives can be an advantage in a pandemic [12]. Ongoing reviews of syndrome definitions, regular refresher training for physicians who report syndromes and review of syndromic trends can improve the accuracy of syndromic surveillance systems.

Syndromic surveillance in Pacific Island countries:

The International Health Regulation (IHR) mandates member countries to establish legislation, policies and systems for the surveillance of infectious diseases that can cause outbreaks and potentially cross international borders [13]. The IHR regulation ensures that every country has its list of infectious diseases required by law for monitoring. Unfortunately, countries in the Pacific have been unable to fulfil their IHR responsibilities because the recommended systems are replicated from more developed countries and require overseas laboratory testing of samples, resulting in delayed responses to possible outbreaks [14]. In 2010, a simplified surveillance system based on syndrome definitions that use clinical signs and symptoms, termed the Pacific Syndromic Surveillance System (PSSS) was proposed and successfully trialed in three Pacific Island countries and later implemented in 21 Pacific Island countries [13,14].

Twenty-one countries in the Pacific region presently use the PSSS, including the FSM. This simplified syndromic surveillance is affordable and sustainable. Furthermore, this initiative has

enabled small island countries in the Pacific to fulfil their IHR obligations. The Pohnpei State Hospital uses the PSSS to monitor and respond to disease outbreaks. In 2019 the Pohnpei State Department of Health and Social Services digitised the syndromic surveillance system. Improving the syndromic surveillance system in Pohnpei is aimed at overcoming challenges such as late data input, incomplete reporting, slow response to outbreak investigation and poor-quality data [14].

Association between rainfall and diarrhoeal illnesses:

Studies assessing the association between rainfall and diarrhoea have shown mixed results. A review by Ghazani et al. [1] showed that high precipitation was associated with an increased incidence of diarrhoea in some places, while low rainfall correlated with increased diarrhoea cases in others. Both low and high rainfalls were linked to increased diarrhoea cases. This trend was not surprising since heavy flooding and drought can lead to diarrhoeal outbreaks. For example, extreme drought led to outbreaks of diarrheal illnesses and eye infections in the Marshall Islands in 2013 [15]. Other studies assessing seasonal diarrhoea suggest that rain events may influence the seasonal presence of rotavirus, directly influencing the seasonal trend in diarrhoea cases (16–18). Diarrhoea is not associated with rain events in areas where rotavirus is not seasonal [6].

Rainfall as a single factor may not be linked to diarrhoea but requires the added multiplying effect of other weather factors, such as temperature or humidity [16,18]. As one review showed, a one-centimetre increase in rainfall plus an increase in temperature of one degree Celsius was associated with a 10% reduction in the incidence of rotavirus [16] and thereby affecting the trend of diarrhoea cases. The results of the aforementioned studies indicate water and sanitation as common themes. Indeed, regardless of weather changes, Njuguna et al. [19] suggest water and sanitation practices as the critical risk factors for diarrhoeal outbreaks.

Association between rainfall and febrile illnesses:

Increased rainfall can also affect the habitat of vectors and influence the trend of infectious diseases [4]. Assessing the correlation between the trend of febrile illnesses and rainfall can provide the evidence needed to plan for outbreaks that may arise because of changes in local weather patterns. Common febrile infections associated with rain events include dengue, leptospirosis and enteric fever [20-22]. Rainfall variation can also influence hepatitis E virus infection [23]. It is unknown if the volume of rainfall affects the trends of dengue, leptospirosis or other febrile illnesses.

Most studies show a positive correlation between dengue, leptospirosis and rainfall, with

a lag time of two to three weeks [24-28]. Furthermore, these trends appear to have seasonal variations following the rainy or monsoon seasons [29,30]. On the other hand, some studies do not show a correlation between dengue fever or leptospirosis with rainfall [31,32]. The differences could be due to reasonable vector control or good ecological management of vectors in these countries. Environmental factors such as soil conditions could also contribute to leptospirosis [33].

Leptospirosis is a frequent cause of febrile illness in the FSM and is commonly associated with dogs, pigs and rats [34,35]. The condition typically presents as a febrile illness with joint aches and pain, and outbreaks can sometimes occur one to two weeks after heavy rainfall. A study in India showed leptospirosis has a seasonal trend and peaked one month after heavy rainfall [28]. However, similar correlation studies have not been done in the FSM or other Pacific island countries.

Predictive models generated from syndromic surveillance data can help predict seasonal trends. Such tools can help manage the impacts of climate change on infectious disease trends. For example, predictive models for leptospirosis in India showed a correlation between monthly rainfall and incidences of leptospirosis [21]. The association was predictable but had a variability of 80% [21]. Their models could not accurately predict July to August of 2011 but accurately predicted the number of leptospirosis cases for August 2013 and August 2014 [21]. The study's prediction model did not include other elements, such as oxygen and iron concentrations in the soil, water and soil pH, human activities and cyclone data, which influence leptospirosis transmission and may have affected the accuracy of the statistical models [21]. The results suggest forecasting models for climate-sensitive infectious diseases may need to include multiple meteorological and geographical factors in the statistical models for better predictive accuracy.

Infectious diseases transmitted by mosquitoes are sensitive to rainfall. Dengue and lymphatic filariasis, two mosquito-borne infections, are endemic in FSM, and the frequency of these infections is related to rainfall [4]. Kosrae, a state of the FSM, has experienced periodic dengue outbreaks. The sporadic outbreaks were most likely related to the vector population's rise and fall. However, until 2013, no reliable data existed on the dengue vector population in Kosrae [36]. Studies in Africa showed malaria positively correlated with rainfall, where parasite density fluctuated with the volume of rain [37]. Similar correlation studies are lacking in PNG and other Pacific countries, although infections such as dengue, malaria and other mosquito-borne infections are common.

Febrile and diarrheal illnesses have been identified as climate-sensitive diseases in the Pacific [4[. But climate change's potential infectious disease-related health impacts

remain under-researched. One way to plan and manage climate-change-related impacts of infectious diseases is to strengthen disease surveillance systems. A robust surveillance system can help monitor infectious disease trends and facilitate timely responses. Routine surveillance data must be regularly evaluated to gather reliable evidence to help plan for climate change-related shifts in disease trends.

Association between rainfall and influenza-like-illnesses:

Influenza-like illnesses and other respiratory illnesses generally have seasonal trends. Within the context of climate change, respiratory illnesses' seasonal trends may change due to changing weather patterns. Influenza-like illnesses have been identified in the FSM as climate-sensitive diseases [4]. Research evidence suggests that ILIs and other respiratory diseases, such as pneumonia, are influenced by temperature and humidity [3,38-40]. Respiratory syncytial virus, a common cause of ILIs, is more active in colder months [7]. A study in PNG assessing pneumonia in children less than five years of age showed that the risk of pneumonia is variable between rainy and drier months of the year [39]. The risk of pneumonia was inconsistent across the different provinces studied [39]. The observation by Kim et al. [39] suggests that the correlation between rainfall and childhood pneumonia in PNG may be geography-specific.

Rainfall appears to influence ILIs and respiratory illnesses, but the available research assessing the correlation between ILIs and weather parameters indicates the relationship is not linear [41]. Human activities that affect the environment or social activities influenced by weather may determine seasonal trends of respiratory diseases in a community.

Understanding the local variation of mosquito populations with rainfall will enhance the environmental management of mosquito transmitted febrile illness. Mosquito populations tend to go up and down following rain events. Ongoing surveillance of febrile syndromes and integration with weather monitoring systems may detect potential early signals of an outbreak.

Continued efforts to eliminate lymphatic filariasis in FSM are ongoing. However, intense transmission continues in the small outer atoll islands [42]. In addition to mass drug administration to eliminate lymphatic filariasis, controlling mosquito breeding sites is a proven preventive strategy.

Association between weather and COVID-19:

Some research suggests that weather variables may influence COVID-19 transmission. For example, a study in Pakistan used Spearman rank correlation analysis to assess the correlation between COVID-19 and meteorological factors such as temperature, humidity and rainfall [41]. That study showed

variation in the correlation across different cities in Pakistan [41]. Humidity was negatively associated with COVID-19 in all towns except Karachi, where it was positively related [41]. Rainfall was positively associated with COVID-19 in all cities studied except in the cities of Islamabad and Peshawar [41]. However, other studies do not confirm or show similar results, prompting calls for robust research designs to examine the relationship between COVID-19 and weather factors [43]. Well-designed studies are needed to identify the intermediate factors and type of relationship (linear or nonlinear) that weather has with intermediate variables and how the factors interact to influence COVID-19 disease dynamics.

Although the weather may influence COVID-19 transmission, other factors are most likely involved. Among the key issues that need to be considered include data quality, non-environmental factors and COVID-19 distribution in time and space within the context of the epidemic's phase [43].

It is also recommended that COVID-19 predictive models include current understanding of disease transmission dynamics [43].

The relationship between COVID-19 and meteorological factors likely varies between tropical and temperate regions. Socioeconomic and cultural practices may also play a role. Predictive models would need to consider all these factors.

DISCUSSION:

Many infectious diseases are associated with rainfall, either increasing or decreasing soon after rain events. This literature review examined studies evaluating the association between rainfall and diarrhoea, febrile illnesses, ILIs and COVID-19 with a focus in the Asia Pacific Region. Such research is crucial because monitoring climate-sensitive infections may help institute risk mitigation strategies for managing the health impacts of climate change. Climate-sensitive infections are linked to the environment through vectors and seasonal changes in the local weather. Systemic surveillance of infectious syndromes aids the assessment of trends and can serve as an early warning system. Additionally, combining syndromic surveillance trends with meteorological variables can provide evidence to inform policy development, health promotion and health service planning. Such approaches will strengthen health systems to be more responsive, resilient and adaptable to climate change.

The evidence reviewed suggests that although infectious disease syndromes may be associated with rainfall, the relation is complex with the interplay of multiple factors. Some research suggests diarrhoea, ILIs, and febrile illnesses may be positively associated with rain, but other studies do not show this association. The positive association is more evident in regions with distinct seasonal rainfall, such as

monsoon seasons. What has emerged from this review is that although infectious syndromes may correlate with rainy seasons or rain events, other local weather variables such as temperature and humidity should also be considered in the analysis. Environmental factors such as soil parameters and geographical terrain may influence infection trends. The present state of research in this area is still poorly understood. It presents opportunities for more research into climate-sensitive infections in the Pacific region, where the effects of climate change may be profound.

CONCLUSION:

Association between rainfall and climate-sensitive infections is multifactorial and geography-specific. Conclusions from studies in one geographical region cannot be applied globally. Further research is needed in Pacific island countries to examine the association between rainfall patterns and potential climate-sensitive infections in order to generate data that is country specific and locally relevant.

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SHORT COMMUNICATION:

VENOUS THROMBOEMBOLISM PROPHYLAXIS IN GERIATRICS INPATIENTS

Running Title: **Venous thromboembolism prophylaxis Geriatrics**

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ABSTRACT:
Venous thromboembolism (VTE) is one of the significant causes of morbidity and mortality for hospital inpatients. The use of VTE prophylaxis in high-risk patients admitted under Geriatric Medicine in RIPAS Hospital, Brunei was evaluated. The electronic medical records of all patients admitted under Geriatric Medicine between 1st February 2022 and 28th February 2022 were reviewed. For these patients, the risk of developing VTE, bleeding risk and whether they were prescribed VTE prophylaxis were assessed. There were 34 patients identified, of which 20 (58.8%) were female. Median age was 81 years, ranging from 64 to 93 years. There were 13 (38.2%) COVID-positive patients, of which 9 (69.2%) were considered high VTE risk. Among these 9 patients, 4 (44.4%) were low bleed risk; of these 4 patients only two were prescribed VTE prophylaxis. Among the 21 non-COVID patients, 17 (80.9%) were high VTE risk. There were 11 (64.7%) with low bleed risk among the 17 patients in the group. Of the 11 patients only 3 (27.3%) were prescribed VTE prophylaxis. The use of VTE prophylaxis among Geriatric Medicine inpatients could be improved. Use of the VTE prophylaxis protocol should be emphasised to clinicians and re-audited to ensure compliance.

Keywords: COVID-19, geriatrics, prophylaxis, risk assessment, venous thromboembolism

INTRODUCTION:

The risk of venous thromboembolism (VTE) increases with age and hospitalisation [1]. Hospital-acquired VTE contributes to significant morbidity and mortality, and cost to the healthcare system[2]. When a VTE risk assessment tool was implemented in England in 2010, there was an associated reduction in VTE-related secondary diagnoses, readmissions to hospital and VTE-related mortality [3]. While this supports the importance of screening and preventing VTE in hospitals, the Epidemiologic International Day for the Evaluation of Patients at Risk for Venous Thromboembolism in the Acute Hospital Care Setting (ENDORSE) study showed that only 58.5% of high-risk surgical

inpatients and 39.5% of medical inpatients were prescribed thromboprophylaxis [4]. The International Medical Prevention Registry on Venous Thromboembolism (IMPROVED) study also showed a similar trend, with only 60% of acutely ill medical patients receiving VTE prophylaxis [5].

COVID-19 infections are known to cause a systemic inflammatory response, leading to a hypercoagulable state and an increased risk of VTE. Anticoagulant treatment has been shown to reduce mortality rate by 60% compared to those without VTE prophylaxis [6]. While studies on VTE prophylaxis in COVID-19 patients remain limited, a systematic review and meta-analysis highlighted the under-prescribing of VTE prophylaxis in admitted patients [7].

Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital is an 880-bedded tertiary hospital in Brunei. Patients aged 70 years and older with 'geriatric syndromes' and complex medical issues are admitted under geriatric medicine. These patients are high-risk of developing VTE, as about half the patients are bedbound or transfers only [8]. As VTE prophylaxis is an important consideration in high-risk patients particularly during the COVID-19 pandemic, its use in patients admitted under Geriatric Medicine in RIPAS Hospital, Brunei was evaluated.

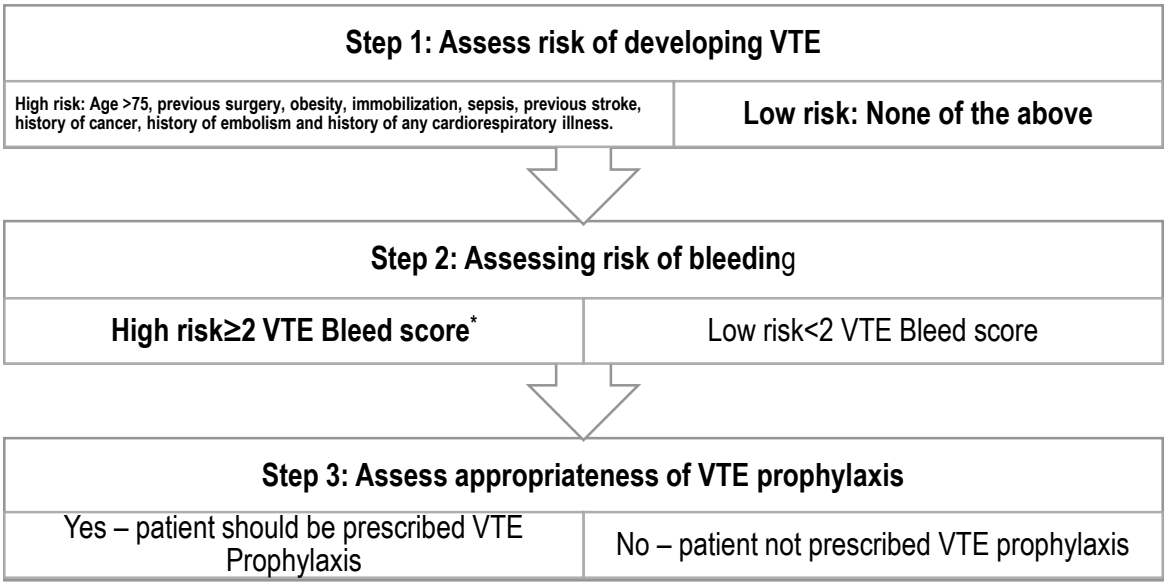
METHODS:

The electronic medical records of all patients admitted under Geriatric Medicine between 1st February 2022 and 28th February 2022 were reviewed. For these patients, the risk of developing VTE based on risk factors [2], bleeding risk using the VTE Bleed score [9], and whether they were prescribed VTE prophylaxis were assessed. The approach of determining whether a patient should be given VTE prophylaxis is summarized in Figure 1. Some patients are high-risk for VTE and bleeding; as the decision of appropriateness is left at the clinician's discretion, compliance with VTE prophylaxis was not reviewed for these patients.

RESULTS:

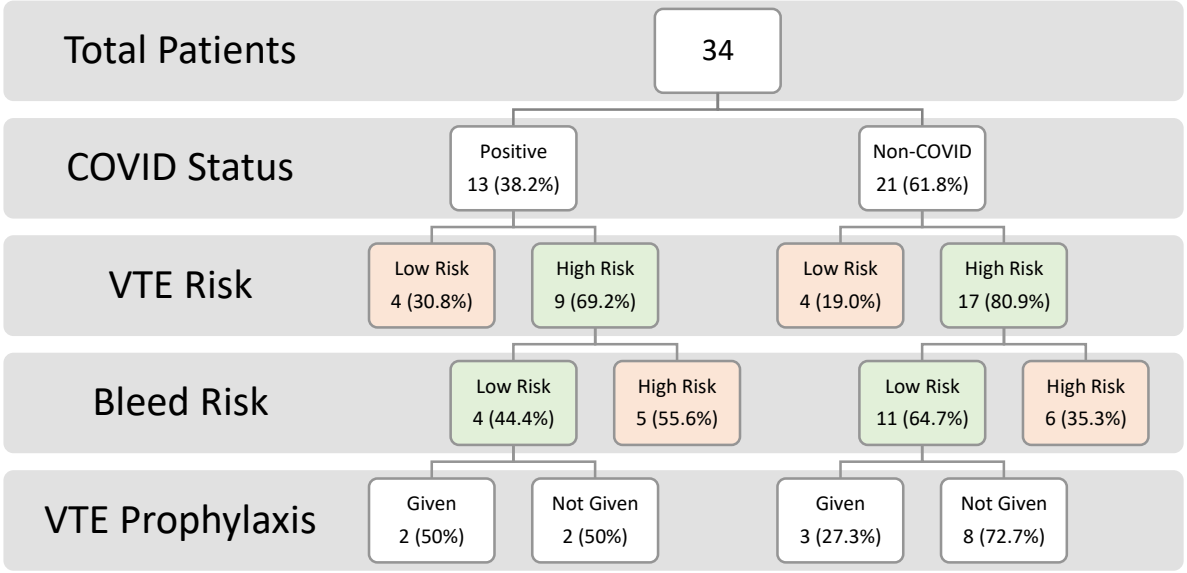
There were 34 patients admitted under Geriatric Medicine in February 2022. There were 20 (58.8%) females. The median age was 81 years, ranging from 64 to 93 years. There were 13 (38.2%) COVID-positive patients, of which 9 (69.2%) were considered high VTE risk. Among these 9 patients 4 (44.4%) were low bleed risk. Two of the 4 patients only were prescribed VTE prophylaxis. Among the 21 (61.8%) non-COVID patients, 17 (80.9%) were high VTE risk. There were 11 (64.7%) with low bleed risk among the 17 patients in this group. Of the 11 patients only 3 (27.3%) were prescribed VTE prophylaxis. The breakdown of patients is summarised in Figure 2.

Figure 1: Decision-making tool to determine appropriateness of VTE prophylaxis



*VTE Bleed Score: Active cancer, male with uncontrolled hypertension, anaemia, bleeding history, renal dysfunction, age ≥60 years [9]

Figure 2: Patients based on COVID status, risk of VTE and bleeding, and whether VTE prophylaxis was prescribed



DISCUSSION:

When Geriatric patients admitted to RIPAS Hospital during the month of February 2022 were audited, it was found that almost three-quarters of the non-COVID patients who were high risk for VTE and low risk of bleeding were not prescribed VTE prophylaxis. This suggests that there is a need to improve this aspect of inpatient management. The CURVE study from Canada showed that among the 90% of acutely unwell patients that should receive VTE prophylaxis, only 16% did [10]. The multinational IMPROVE study showed that almost half the patients were eligible for VTE prophylaxis, but this was prescribed in only 60% of these patients [5].

For COVID-19 geriatrics patients, 50% of those with high VTE risk but low bleed risk were given prophylaxis. While these numbers are small, this still indicates significant room for improvement, given the pro-thrombotic state of COVID-19 infections and associated inflammation [7]. The main limitation of this audit is the small number of patients, which precludes further analysis of local factors which are associated with higher risk of VTE or bleeding. This may offer further information regarding prevention or risk modification, and should be considered for future studies.

Based on these findings, the following action steps are recommended: to raise awareness of VTE risk-stratification and prophylaxis, develop flow-chart or checklist to decide which geriatric patient should be prescribed VTE prophylaxis, and to assess whether there is improvement in VTE prophylaxis prescriptions with these interventions.

CONCLUSION:

The use of VTE prophylaxis among Geriatric Medicine inpatients could be improved. Use of the VTE prophylaxis protocol should be emphasised to clinicians and re-audited to ensure compliance.

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SHORT COMMUNICATION:

DEMENTIA KNOWLEDGE AMONG MEDICAL AND DENTAL STUDENTS IN UNIVERSITI BRUNEI DARUSSALAM

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Dementia is one of the main causes of disability and dependence in older people. The World Health Organisation (WHO) global action plan on the public response to dementia 2017-2025 was developed with seven action areas. The action area regarding dementia diagnosis, treatment, care and support emphasizes the importance of improving the knowledge and skills of healthcare providers [1]. Teaching of dementia core competencies should start in the undergraduate years.

The "mental health Gap Action Programme" (mhGAP), also developed by the WHO, offers training resources for non-specialised health professionals to manage mental health conditions, including dementia. The effectiveness of the mhGAP programme was shown to be affected by cultural differences and attitudes towards mental health, as well as the level of education, knowledge and skills of the participants [2].

In Brunei, the Geriatric Medicine specialty in Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital provides teaching sessions to undergraduate medical and dental students from Universiti Brunei Darussalam (UBD) regarding ageing-related topics, including dementia. Their baseline knowledge was assessed using the quiz from the mhGAP dementia module [3].

This descriptive cross-sectional study was carried out among undergraduate medical and dental students from UBD attending the geriatrics block session held in January 2022. The quiz was accessed by the students via an online link prior to their virtual lectures during the geriatrics modules. The lectures were delivered online using the Zoom platform to the combined group of second year dental, second year medical and third year medical students due to the COVID-19 pandemic.

There were 61 participants in total, consisting of 9 (14.8%) second year dental students, 27 (44.3%) second year medical students, and 25 (41.0%) third year medical students.

Overall, the mean knowledge score was 84.3%, with the majority (72.1%) having good knowledge about dementia and scoring above 80% in the quiz. The majority were aware that dementia is a chronic progressive syndrome, the impact of dementia on society, and that with early recognition and support, the lives of people with dementia and their caregivers can be improved. However, more knowledge on the different management approaches for dementia was required, including psychosocial interventions. Interestingly, the second year medical students performed better in some aspects of the quiz compared to the third year students. However, the relatively small numbers of questions and limited variability of responses precluded more detailed analysis to further elucidate the differences between groups. A longer questionnaire applied to a larger number of participants in each group should be considered to evaluate the differences between the student groups. The questions and responses to the mhGAP dementia quiz are included as an Appendix.

A study of senior medical students who rotated through the US Department of Veterans Affairs Memory Disorders Clinic at the Central Arkansas Veterans Healthcare System, Little Rock identified prevalent dementia knowledge gaps, which were improved through an interdisciplinary geriatric educational experience [4]. A comparative study of Chinese nursing and medical students found that while medical students had higher dementia knowledge scores than nurses, there were no differences in scores for the Approach to Advanced Dementia Care Questionnaire (ADCQ) between medical and nursing students. More concerning was the lack of application of a person-centred care approach [5].

Putting together the findings of our study, while there are Action Plans and training tools such as mhGAP available, there is a need to improve the knowledge base regarding dementia management. Further work is required to evaluate how dementia knowledge can be translated to action, as application to clinical practice of multidisciplinary, person-centred care for people with dementia.

Conflicts of Interest: The authors have no conflicts of interests to declare.

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Appendix. Questions and Responses to mhGAP dementia quiz

No	Questions and Answer Options	Y2 Dent N = 9	Y2 Med N = 27	Y3 Med N = 25	Total N = 61
		N (%)	N (%)	N (%)	N (%)
1.	**Which of the following is a common presentation of dementia?**				
	Low mood and loss of enjoyment in usual activities.	0	0	1 (4%)	1(1.6%)
	Fixed false beliefs and hearing voices.	0	0	2 (8%)	2 (3.3%)
	Excessive hyperactivity and inattention.	0	0	0	0 (0%)
	Decline or problems with memory and orientation.	9 (100%)	*27 (100%)*	*22 (88%)*	*58 (95.1%)*
2.	**Which of the following is a common presentation of dementia?**				
	Severe forgetfulness and difficulties carrying out usual work, domestic or social activities.	7 (77.8%)	25 (92.6%)	22 (88%)	54 (88.5%)
	Drowsiness and weakness down one side of the body.	0	0	0	0 (0%)
	Fluctuating mental state characterized by disturbed attention that develops over a short period of time.	1 (11.1%)	2 (7.4%)	3 (12%)	6 (9.8%)
	Low mood in the context of major loss or bereavement.	1 (11.1%)	0	0	1 (1.6%)
3.	**Which of the following is the best description of dementia?**				
	Dementia is a communicable disease of the brain that can be contagious.	0	0	0	0 (0%)
	Dementia is most common in those aged 40–50 years old, and rare after this age.	0	0	1 (4%)	1 (1.6%)
	Dementia is a chronic and progressive syndrome due to changes in the brain.	*9 (100%)*	*27 (100%)*	*24 (96%)*	*60 (98.4%)*
	Dementia is rarely noticed by anyone other than the person who has it.	0	0	0	0 (0%)
4.	**Which of the following is the best description of dementia?**				
	Dementia can have a large impact on the person, their carer, family and society at large.	*8 (88.9%)*	*24 (88.9%)*	*24 (96%)*	*56 (91.8%)*
	Dementia can be cured through pharmacological interventions.	0	0	1 (4%)	1 (1.6%)
	Dementia does not interfere with activities of daily living, such as washing, dressing, eating, personal hygiene and toilet activities.	0	0	0	0 (0%)
	Dementia is a normal part of ageing.	1 (11.1%)	3 (11.1%)	0	4 (6.6%)
5.	**Which of the following is a common cluster of symptoms in dementia?**				
	Minimally responsive, slow respiratory rate and pinpoint pupils.	0	1 (3.7%)	1 (4%)	2 (3.3%)
	Problems with orientation, mood and emotional control.	*3 (33.3%)*	*16 (59.3%)*	*19 (76%)*	*38 (62.3%)*
	Failure to thrive, poor motor tone, delay in reading and writing.	6 (66.7%)	10 (37.0%)	5 (20%)	21 (34.4%)
	Elevated mood, decreased need for sleep, increased activity.	0	0	0	0 (0%)
6.	**Which of the following is a common cluster of symptoms in dementia?**				
	Excessive over-activity and inattention.	0	0	0	0 (0%)
	Excessive crying, clinging to a carer and extreme shyness.	0	0	1 (4%)	1 (1.6%)
	Abrupt onset and disturbed level of consciousness.	0	0	0	0 (0%)
	Decline of memory with mood or behavioural problems.	*9 (100%)*	*27 (100%)*	*24 (96%)*	*60 (98.4%)*
7.	**Which of the following statements best describes treatment options in dementia?**				
	All people with dementia should have access to pharmacological interventions, regardless of specialist availability.	0	0	1 (4%)	1 (1.6%)
	Pharmacological interventions, if started early enough, can cure dementia.	0	0	0	0 (0%)
	With early recognition and support, the lives of people with dementia and their carers can be significantly improved.	*8 (88.9%)*	*24 (88.9%)*	*23 (92%)*	*55 (90.2%)*
	Psychosocial interventions for dementia should only be provided by a specialist, due to their complexity.	1 (11.1%)	3 (11.1%)	1 (4%)	5 (8.2%)
8.	**Which of the following might you do first for a carer of someone with dementia?**				
	Provide them with antipsychotic medication to administer to the person if their behaviour is unmanageable.	1 (11.1%)	1 (3.7%)	0	2 (3.3%)
	Provide them with details of specialists, to see if the person can be started on medication.	3 (33.3%)	1 (3.7%)	3 (12%)	7 (11.5%)

	Assess their needs, including whether they are coping or becoming depressed.	*4 (44.4%)*	*25 (92.6%)*	*20 (80%)*	*49 (80.3%)*
	Refer them to a social worker who can assess whether they are experiencing financial hardship.	1 (11.1%)	0	2 (8%)	3 (4.9%)
9.	**Which of the following is the best first-line treatment for someone with dementia?**				
	Pharmacological interventions.	1 (11.1%)	3 (11.1%)	5 (20%)	9 (14.8%)
	Psychosocial interventions.	*6 (66.7%)*	*19 (70.4%)*	*19 (76%)*	*40 (65.6%)*
	Antipsychotic medication.	0	3 (11.1%)	1 (4%)	8 (13.1%)
	Referring to a specialist.	2 (22.2%)	2 (7.4%)	0	4 (6.6%)
10.	**Which of the following are components of psychosocial intervention in dementia?**				
	Interpersonal therapy in combination with cognitive behavioural therapy.	6 (66.7%)	8 (29.6%)	7 (28%)	21 (34.4%)
	Promoting independence and support for the person with dementia, including ways to improve cognitive functioning.	*3 (33.3%)*	*16 (59.3%)*	*17 (68%)*	*36 (59.0%)*
	Cholinesterase inhibitors, in combination with antipsychotics if there are behavioural and/or psychological symptoms.	0	1 (3.7%)	1 (4%)	2 (3.3%)
	Reducing physical activity, changing their usual routine and leaving things exactly as they are in the house.	0	2 (7.4%)	0	2 (3.3%)
11.	**Which of the following might you tell a carer of someone with dementia?**				
	The person with dementia will only get worse so you should not bother trying to help them.	0	0	0	0 (0%)
	A lot can be done to make the person with dementia more comfortable and to make providing support less stressful.	*9 (100%)*	*26 (96.3%)*	*25 (100%)*	*60 (98.4%)*
	Taking the person to new and unfamiliar places can help stimulate their memory.	0	1 (3.7%)	0	1 (1.6%)
	The person with dementia should avoid physical and recreational activities to help preserve their health.	0	0	0	0 (0%)

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