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Original Article

Unveiling Co-Infections: Hepatitis C Virus And Malaria Sero-Prevalence Among Outpatients Attending General Hospital Wukari In Taraba State, Nigeria

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Abstract

Malaria and hepatitis C virus (HCV) infections are significant public health challenges when they overlap geographic distributions. There is potential for co-infections and syndemism of both pathogens due to the rising incidence of the overlap between regions endemic for hepatitis C virus and malaria. Hence, the aim of this study was to determine the sero-prevalence of Hepatitis C virus (HCV) and malaria co-infection among outpatients attending General Hospital Wukari, Taraba State, Nigeria. A total of 100 outpatients consisting of 30 males and 70 females within the age of 11 to 70 years were randomly recruited to the study. Rapid diagnostic test kits were used to screen for HCV and malaria among the outpatients. Of the 100 outpatients screened, 12 (12%) were sero-positive for HCV while 4(4%) were sero-positive for Malaria. Of the 12 HCV sero-positive patients, 4 (13.33%) were male while 8 (11.43%) were females. Furthermore, all malaria sero-positive patients were male. Likewise, malaria and HCV co-infection in this study was 2%. Although low, the prevalence of HCV infection, malaria and HCV-malaria co-infection are worrisome especially in this area. Hence, patients should be encouraged to go for routine screening and know their infection status so as to prevent complications due to active infection.

Keywords: Co-infection, Hepatitis C, Malaria, Wukari.

Introduction

Infectious diseases are one of the main sources of suffering for people worldwide. Malaria and hepatitis C virus (HCV) infections are two of these illnesses that have disproportionately harmed individuals [1]. The synergy between malaria and other viral diseases co-infections involving human parvovirus B19 with malaria, hepatitis B virus, and human immunodeficiency virus and human immunodeficiency virus, has been demonstrated by a number of epidemiologic data to far [2]. Research on the consequences of malaria and HCV co-infections on afflicted hosts, however, is scarce. According to reports, there are about 180 million HCV-positive people in the world [3]. While the

prevalence of HCV is less than 3% worldwide, reports of prevalence in some regions of the world approach 15% [4]. For example, epidemiologic data showed a frequency of more than 14% in Egypt [4]. There are several genotypes of the hepatitis C virus, and their global distribution varies. The genotypes 1a, 1b, 2a, and 3a of the hepatitis C virus are commonly referred to as the epidemic subtypes due to their widespread distribution and higher percentage of HCV cases, especially in industrialized nations [5]. Before the development of pathogen sequencing technology, these HCV genotypes were probably transmitted between three and four decades ago by injectable drug users and blood transfusions [6,7]. The so-called endemic strains, on the other hand, are comparatively uncommon and have long been restricted to particular areas, including Southeastern Asia, West and Central Africa, and Southern Asia [8,9].

The five areas of the World Health Organization (WHO) are all impacted by the pervasive problem of malaria transmission. Roughly 3.2 billion people have a higher than 1:1000 probability of contracting malaria annually and are susceptible to infection with Plasmodium spp. [10]. According to the 2015 World Malaria Report, there were around 214 million cases of malaria and 438 000 malaria-related fatalities. These numbers indicate a decline of 37% and 60%, respectively, in malaria cases and deaths during a 15-year period. Approximately, 90% of malaria-related deaths happened in the sub-Saharan African region, which bore the brunt of the disease. According to the WHO [10], children under the age of five accounted for two thirds of these deaths.

Infection with parasites belonging to the genus Plasmodium causes malaria. According to Ashley *et al.* [11], there are six Plasmodium species that cause malaria in humans: *P. falciparum*, *P. malariae*, *P. ovale curtisi*, *P. ovale wallikeri*, *P. vivax*, and *P. knowlesi*. There are certain similarities between the pathogenesis of Plasmodium spp. and HCV, which cause malaria and hepatitis C, respectively, particularly when they are developing inside the liver cells [12]. While the co-infection of HCV and malaria is mainly unknown, susceptible individuals may be able to catch both infections because of their comparable epidemiology. According to current study, heparan sulphate proteoglycans (HSPGs), apolipoprotein E, CD81, and scavenger receptor B1 (SR-B1) are the four host receptors that Plasmodium spp. and HCV use to enter hepatocytes [13]. In locations where malaria transmission is high, co-infections, and syndemism are expected to develop due to the rising incidence of HCV infections in these regions. Therefore, concurrent infections with both viruses could occur.

15% to 20% of HCV-positive individuals experience spontaneous viral clearance, while the remaining individuals develop chronicity [14]. According to Lauer and Walker [15], persistent HCV infections are typically linked to the development of liver steatosis, cirrhosis, hepatocellular cancer, liver failure, and eventually, death. Over the next 20 years, mortality indirectly related to HCV infections will raise in industrialized countries as the incidence of HCV infections looks to be declining [16]. Therefore, developing methods to prevent new co-infections that could exacerbate the clinical presentation requires a solid understanding of HCV infection.

On the other hand, severe plasmodiasis involving the liver frequently contributes significantly to human illness and mortality. Jaundice typically indicates a certain level of liver impairment in individuals with malaria [17]. According to reports from endemic countries, jaundice can result from 2.5%

to 5.3% of malaria infections due to Plasmodium falciparum [18]. Even though hepatic dysfunction is uncommon in malaria patients, falciparum plasmodiasis patients are reporting an increasing number of instances. According to Bhalla *et al.* [19], there is a spectrum of liver dysfunction ranging from modest abnormal liver function tests (LFTs) to liver failure. Individuals suffering from malaria who also have varying degrees of liver damage are more likely to experience consequences from HCV co-infections.

Treatment that is both correct and timely is essential to preventing or reducing the serious effects of co-infections. Currently, no antimalarial medication is able to completely destroy every stage of the parasite's life cycle [20]. As a result, to effectively battle malaria, one or more of the four medication types are frequently administered concurrently [21]. Treatment plans also depend on the Plasmodium species, the malaria's geographic location, and the disease's severity [22]. After the parasite is removed from the body, malaria-related hepatitis frequently goes away, and three days after therapy begins, serum bilirubin levels typically start to drop. Yet, this might cause people who have co-infections or comorbidities to experience a delay [23].

With the long-standing treatment for hepatitis C virus infections, people are becoming less susceptible to cirrhosis or hepatocellular carcinoma and in some instances successfully cleared HCV from their body systems. Thus, the purpose of this study was to ascertain the seroprevalence of malaria and HCV co-infection among people living in Wukari, Taraba State, Nigeria.

Materials and Methods

Study Area

Taraba State, Nigeria has the Local Government Area of Wukari. The town of Wukari is home to its headquarters. As of the 2006 census, its area was 4,308 km^2, and its population was 241,546[24]. The area's postal code is 670. Jukun is the language used locally (Wapan, Jibu, Nyifon). Wukari is located between longitude 9047'59" East and latitude 7055'42" North. Jukun, Kutep, Tiv, Hausa, and Fulani are the principal languages spoken there [25].

Study Design and Sampling

The study adopted a hospital-based prospective study, involving one-hundred (100) randomly sampled outpatients attending General Hospital Wukari, Taraba State. Blood samples for Hepatitis C and malaria test were collected and tested after patient's consent were sought.

Ethical Approval

Along with a letter of introduction from the Department of Microbiology at Federal University Wukari, ethical approval was acquired from the Taraba State Ministry of Health and the Wukari General Hospital management. Prior to obtaining verbal assent, outpatients were duly informed about the study's aims.

Materials

The materials used for this study include blood samples, syringes and needles, sterile EDTA and plain tubes, hand gloves, tourniquet, dry and wet cotton swabs, centrifuge, refrigerator, and rapid diagnostic test (RTD) kits.

Sample Collection

Venous blood samples were collected from patients using a sterile syringe and needle; and dispensed into an EDTA or plain sample container for Malaria parasite and Hepatitis C tests respectively.

Analysis of Samples for Hepatitis C Virus

Samples were tested for the presence of antibodies to HCV using the HCV rapid test strip. The blood samples were centrifuged for efficient separation. Two drops of plasma were added to the sample pad using disposable pipette in the kit. The result was read within 10 min [26].

Interpretation of Results for Hepatitis C Virus

Sero-negative samples only show one line at the control region, whereas two lines emerged on the test and control regions, respectively, for sero-positive samples.

Analysis of Samples for Malaria Test

Samples were tested for the presence of antibodies to Malaria parasite using a Standard Diagnostic Inc. Rapid Diagnostic Test (RDT) strip. A drop of whole blood was applied to the sample pad on the test card along with two drops of buffer. Results were read after 15 minutes.

Interpretation of results for malaria test

Sero-negative samples only show one line at the control region, whereas two lines emerged on the test and control regions, respectively, for sero-positive samples.

Statistical Analysis

Tables created using Microsoft Excel (2016) were used to display the data that were produced during the investigation. To assess the difference between categorical variables, the p-value and chi-square statistic were calculated at a 95% confidence range. For a p-value of less than 0.05 ($p < 0.05$), the difference was considered significant.

Results and Discussion

This study investigated the sero-prevalence of Hepatitis C and malaria co-infection among patients in Wukari Local Government Area of Taraba State. According to reports, plasmodium and hepatitis C virus co-illnesses are frequent in a number of tropical regions, and both infection's endemic ranges frequently overlap [27]. In addition, it has been demonstrated that co-infection with HCV and malaria can affect how quickly either hepatitis or malaria, or both, advance [28].

In Table 1, the "X2" values represent the chi-square ($\chi 2$) statistics for each variable:

For HCV: X2 = 0.0722.

For Malaria: X2 = 8.2589.

These values quantify the degree of association between gender and the prevalence of each disease. A higher chi-square value suggests a stronger association between the variables. The p-value associated with each variable indicates the probability of observing the data under the assumption of no association between gender and disease prevalence:

For HCV: *P*-value = 0.788232

For Malaria: *P*-value = 0.004055

These p-values help determine the statistical significance of the association. In this case, for HCV, the p-value is 0.788232 which is greater than the commonly used significance level of 0.05, suggesting no statistically significant association between gender and HCV prevalence. However, for Malaria, the p-

value is 0.004055 which is less than 0.05, indicating a statistically significant association between gender and malaria prevalence.

A total of 100 patients were sampled including 30 males and 70 females. 12 (12%) of the 100 subjects were positive for Hepatitis C Virus (HCV) of which 4 were males with a percentage of 13.33% and 8 were females with a percentage of 11.43%. Furthermore, only 4 patients tested positive for the Malaria parasite of which all 4 were males and have a percentage of 4% (Table I, Figure 1).

Table 1 Gender based prevalence of HCV and malaria parasite

Variables	Females(n=70)		Males(n=30)		Total	X^2	*P*-value
	+n(%)	-n(%)	+n(%)	-n(%)			
HCV	8(11.43)	62(88.57)	4(13.33)	26(86.67)	12(12)	0.0722	0.788232
Malaria	0(0.0)	70(100.0)	4(13.33)	26(88.67)	4(4)	8.2589	0.004055*

**- Statistically significant*

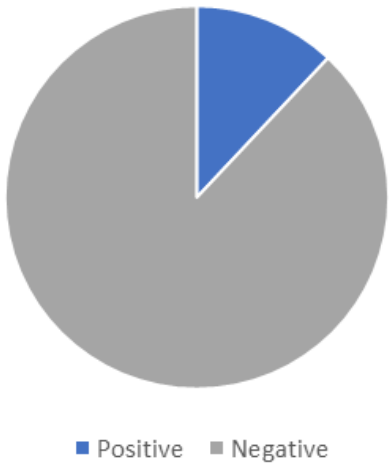

Figure 1 Pie chart showing overall prevalence of HCV among study participants

From the present study, HCV sero-prevalence was 12%. This is higher than the 6.0% reported in Wukari [25] and 6.5% reported in Kano [28]. The prevalence is however similar to 11% reported in Kogi State [29], 11.5% reported in Ekiti State [30] and 12.3% reported in Katsina [31]. Olayinka *et al.* [32] observed that the incidence of chronic HCV infection has been declining, primarily as a result of HCV vaccination and enhanced health-care procedures such as blood and blood product screening, safe injection techniques, and infection control policies and procedures.

Table 2 presents the distribution of malaria infection among different age groups. The highest prevalence of malaria was noted among patients between 21-30 (100%) years while the other age groups had zero prevalence of malaria. The prevalence of malaria infection was significantly different between genders as the only two persons positive for malaria were both males (Figure 2).

Table 2 also shows the distribution of HCV infection among age groups. The highest prevalence was seen among patients between 21-30years (50%), followed by 11-20 years, 31-40 years, and 61-70 years, all of whom had a

16.67% prevalence of HCV. Patients between 41-50 years and 51-60 years had zero prevalence of malaria.

Compared to 30.59% and 25.5% reported in Kano [33, 28] and 77.6% reported in Enugu state [34], the 4% prevalence rate of malaria infection in this study is lower. Lower prevalence of malaria in Wukari can be associated with the implementation of measures to curb malaria in spread such as proper sanitation and the use of mosquito nets. Furthermore, males (100%) had greater malaria burden than women (0%). This, however disagrees with Sharif *et al.* [28] who reported a higher prevalence of malaria among females (18%) than males (7.5%).

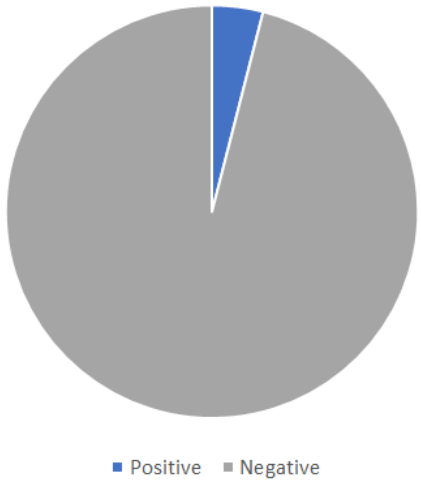

Figure 2 Pie chart showing overall prevalence of malaria among study participants

Table 2 Age based prevalence of malaria and HCV among outpatients

Age group	N	Malaria n(%)	HCV n(%)	X^2	*P*-value
11-20	18	0(0.0)	2(16.67)	1.1111	0.291841
21-30	48	4(100.0)*	6(50.0)	0.4465	0.503996
31-40	18	0(0.0)	2(16.67)	1.1111	0.291841
41-50	6	0(0.0)	0(0.0)	0.00	1.00
51-60	6	0(0.0)	0(0.0)	0.00	1.00
61-70	4	0(0.0)	2(16.67)	1.50	0.220671
Total	100	4(4.0)	12(12.0)	4.3478	0.037056*

Table 3 shows the Sero-prevalencen(the level of a pathogen in a population, as measured in blood serum) of co-infection of HCV and malaria among outpatients. While 4(4%) and 12(12%) were sero-positive for malaria and HCV respectively, only 2(2%) patients had co-infection of malaria and hepatitis C virus.

The 2% co-infection prevalence rate reported in this study was low and this could be connected to the small number of participants (100) that were recruited for the current study. However, it may also indicate that efforts to prevent and treat HCV and malaria are having the desired effect and that the trend of these two infections is declining [28]. In general, co-infection rate variations may result from variations in geographic locations, risk group types, and exposure methods, as multiple studies have documented and predicted in various parts of the world [35,36].

Table 3 Prevalence of malaria and HCV Co-infection among outpatients

Infection	Number of positive (%)	Number of negative (%)
Malaria	4(4)	96(96)
Hepatitis C	12(12)	88(88)
Co-infection	2(2)	98(98)

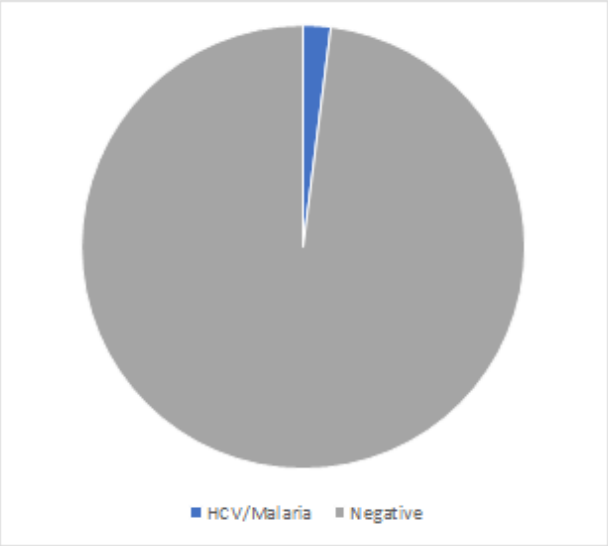

Figure 3 Pie chart showing HCV and Malaria co-infection among study participants

Conclusion

The study of Hepatitis C co-infection with Malaria among individuals in Wukari, Taraba State was seen to have a prevalence rate of 2%. It was also observed that the prevalence of HCV infection was 12% while that of malaria was 4%. The low prevalence of both Hepatitis C Virus and Malaria observed among the 100 patients suggests that campaigns about the prevention and control of HCV and malaria is paying off. This implies that people employ several preventive measures against the disease. Nevertheless, the HCV/Malaria campaign needs to be intensified.

Competing Interest

The authors declare that there is no competing interest in this study.

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Ethical Codes

Good Practice Research

1. It is the responsibility of every researcher at Federal University Wukari to carry out their research in the most

responsible and conscientious way possible, as well as to fulfill obligations to society, their profession, the university, and the people who pay their work. The goal of the university is to promote an atmosphere that values sound research practices and provide sufficient guidance and oversight at all pertinent levels. Department heads and faculty deans have an obligation to make explicit the expectations for research in their departments and related fields and to make sure that following such expectations is normal procedure.

2. Ethical standards and guidelines for research conduct are available from numerous professional societies and research funding organizations. The University anticipates that adherence to this Code of Good Research Practice will satisfy the general standards of these organizations, but in cases where extra specialized requirements are included, University staff members are expected to comply as necessary.

3. *Honesty*: Regardless of discipline or institution, the fundamental component of every research effort is the requirement that researchers be truthful about both their own research activities and how they react to those of other researchers. This is true for all aspects of research, such as designing experiments, collecting, processing, and publishing data, as well as recognizing the direct and indirect contributions of associates, partners, and others.

4. Plagiarism, piracy, and the fabrication of results are unacceptable behaviors for all university staff members. Violations of this policy will be dealt with severely, and the proper university disciplinary procedure will be triggered if necessary.

5. *Openness*: The University encourages researchers to be as transparent as possible when discussing their work with other researchers and the general public, while also acknowledging the necessity for researchers to safeguard their own research interests during the planning and acquisition of their results. When results are published, the University expects researchers to make pertinent data and materials available to others upon request.

6. In addition, the University anticipates that researchers would adhere to any relevant best practices specified in guidelines released by funding agencies, scientific bodies and organizations.

7. Group leadership and cooperation: It is the duty of all senior personnel at the university to establish an environment that promotes ethical research practices. Therefore, it is the responsibility of the group leader to provide a cooperative research environment in which team members are motivated to grow as individuals and where free flow of ideas for study is encouraged. In addition, they have to make sure that research is appropriately directed and that researchers and research students are properly supervised.

8. Researchers must explicitly identify the funding source in their submission and take into account any potential hazards to the university's reputation as well as any ethical ramifications of the funding source.

9. *Data protection:* Researchers must maintain accurate and transparent records of all study techniques followed and conclusions, including preliminary findings, throughout their work. This is required not simply to show that appropriate research practices are followed, but also in the event that inquiries concerning the study's methodology or findings are later made. Similar justifications apply to the need to securely store research-generated material on paper or in electronic format as needed.

10. *Publication of study findings:* Publication of research findings in a suitable format, typically as articles in peer-reviewed journals, is typically a requirement of research funding. This has long been acknowledged as the most effective method for reviewing research findings and results.

11. *Authorship*: In the framework of ethical research practices, authorship is a crucial problem. Anybody named as an author on a paper is expected by the university to take personal responsibility for making sure that they are aware of the paper's contents and can recognize their contributions to it. Honorary authorship is not a proper practice.

12. Acknowledging the involvement of collaborators and other participants - Formal collaborators and anybody else who directly or indirectly supports the research must be duly thanked for their contributions in all areas of the study. This covers all situations where statements regarding the research are made, such as when details about the nature and methodology of the study are shared or the results are published. Ignoring the contributions of others is considered a sign of unprofessional behavior. On the other hand, co-authors and other contributors bear some of the accountability for the study's findings.

13. All community members have a duty to make sure that novice researchers are aware of appropriate research practices, but department heads, group leaders, and research student supervisors are in particular accountable for this.

14. Integrity in submitting research proposals: Principal Investigators and other designated investigators must make every effort to guarantee the completeness and correctness of the data included in grant applications.

15. Integrity in research project management - Principal Investigators and other designated investigators should make every effort to guarantee that project management complies with sponsor, institutional, legal, ethical, and moral requirements.

16. Conflict of Interest - Anybody having any involvement in the management or conduct of research has an obligation to recognize and disclose any conflicts of interest, whether they be of a financial, personal, ethical, moral, or legal kind.

17. It is the duty of principal investigators to guarantee the security and welfare of employees engaged in their projects. They should evaluate the dangers and harm that could arise, and they shouldn't force any researcher to conduct work that could put them in danger of injury-either bodily or psychological.

18. It is the duty of all researchers to think about their personal safety and wellbeing, and they should discuss any worries they may have with their principal investigator or another research manager.

Human Participants Research

1. *Informed consent*: The researcher should, if at all possible, notify prospective participants beforehand of any aspects of the study that could plausibly affect their decision to participate.

2. Written consent should be obtained for sensitive study topics, and the informed consent procedure should be outlined in detail in the ethical protocol.

3. When it comes to minors, parents, guardians, or educators acting in loco parentis may seek informed permission, as well as the minors themselves if they are old enough to understand. However, parents' written informed agreement should be sought when the subject of the study is delicate.

4. As long as sufficient informed consent and debriefing processes are

suggested, it is typically not seen as deception to omit the study's particular goal from the beginning of the participants.

5. When using other techniques to get vital data is not feasible, covert observation is a valid research strategy. Current privacy laws must be followed when doing covert research. If informed consent was not acquired beforehand for covert research conducted in private settings, it should, whenever feasible, be obtained after the fact.

6. Right to withdraw - If at all feasible, participants should be made aware of their freedom to leave the research at any moment and without incurring any fees at the beginning.

7. When it comes to minors, the adults acting in place of parents or the kids themselves, if they can comprehend enough, should be made aware of their ability to opt out of the study.

8. *Protection from injury:* Throughout the course of the study, researchers must make every effort to shield participants from injury, both psychological and bodily.

9. Take notes that although if gaining informed consent (60) is crucial, it does not release the researcher from duty to ensure the participant's safety during stressful or dangerous procedures. Under such circumstances, the participant's protection- such as having access to trained medical assistance-must be outlined in the ethical protocol.

10. If a research practice nevertheless causes physical or mental harm, investigators must act to correct the situation.

11. Where feasible, researchers should give a description of the methodology and goal of the study. If this cannot be provided right now, it should ideally be when the study is finished.

12. Throughout the conduct and reporting of the research, researchers must maintain the confidentiality of the participant's identity and data, unless they have the participant's consent.

13. Procedures for how this will be accomplished may need to be specified in ethics protocols. For instance, the secretary might encrypt the interview transcriptions so that the participant's name and data are never recorded side by side in a written document.

14. Professional bodies' ethical guidelines - This list of guidelines is broad and does not include every factor that should be taken into account in every field. It is imperative to adhere to the rules and principles published by relevant professional groups, and to interpret and expand upon the present principles as deemed required in this particular scenario.

Research Involving Animal Subjects

1. Some biomedical and biological science research areas require animal use until appropriate replacements are available.

2. The dedication to upholding animal welfare in research is the foundation of all projects using animals. As mandated by international best practices, the Committee responsible for supervising animal-related research in each Faculty where it is pertinent should have both lay representation and veterinary and animal care experience.

3. The ethical review procedure guarantees that personnel utilizing animals for research are properly supervised and trained, and that the highest standards of animal care, welfare, and accommodations are upheld.

4. When feasible, substitutes for animal testing should be used, such as tissue culture, computer modeling, cell and molecular biology, and human subjects' research.

5. The primary research animals at the College of Medicine are rats and mice. While other creatures like dogs and even

cats might sometimes be used, this is not a common occurrence.

6. The college of Science's Biological Sciences uses a wider range of animals, including fish, crabs, and insects (such as grasshoppers and mosquitoes) in addition to all kinds of rodents.

7. The departments of zoology, cell biology and genetics, and marine sciences are among the departments in the Faculty of Science that (sub) specialize in the study of animals.

8. In light of the aforementioned, it is necessary to establish the Committee for the Use of Experimental Animals and include the relevant departments.

9. A handbook of guidelines outlining the ethical concerns unique to each FUW REC organ should be released. Researchers will be able to purchase such a booklet at reasonable costs from the Federal University Wukari bookshops. In addition to being a more successful means of raising researchers' knowledge of ethics, it brings in money for the university.

Data Confidentiality and Access

1. Following its existing use in research, researchers should guarantee sufficient open access to primary data arising from publically financed research. Information about identifiable persons must be stored in compliance with data confidentiality laws and any assurances provided to data subjects. Before making such data publicly available, it must be anonymized. If anonymity and secrecy cannot be ensured, researchers may impose an embargo on access.

2. Each study project's "primary data" must be determined by the researchers. Typically, this will be an archived data set, but it could also contain transcripts from interviews, completed questionnaires, lab notebooks, and audio and video recordings.

3. After a research project is finished, the university anticipates that primary research data will be kept safely for ten years, or for as long as a research sponsor may need. It is the responsibility of the University to guarantee the availability of suitable storage facilities. When a staff member transfers to another institution, the non-current primary data from research supported by the University must be kept in storage at the University.

4. Publications resulting from research that is sponsored by the public should, if feasible, be made available via an open access system. Articles should be published as open access wherever feasible and should be placed in the University research repository in compliance with the most recent rules.

5. Other research reports ought to be freely accessible, unless official or commercial confidentiality regulations prohibit it.

6. Should human tissue samples be shared and exchanged with foreign partners, a Materials Transfer Agreement must be signed by the appropriate authorities at the home institution and the receiver organization located outside of Nigeria. The guidelines and suggestions of the National Code for Health Research Ethics will be followed when performing an MTA concerning research involving human subjects.

7. Research activities have to adhere to the National instructions on Research Ethics (including the National Code of Health Research Ethics and the instructions of the National Health Research Ethics Committee) and any data protection regulations. Any ramifications of the intellectual property laws of Federal University Wukari must be carefully considered.

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