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THE CHRONIC KIDNEY DISEASE OF UNKNOWN AETIOLOGY (CKDu) EPIDEMICS IN NORTHERN YOBE STATE: THE MISSING RESEARCH GAP

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ABSTRACT

Bade community in Northern Yobe State has been known as a 'hotspot' of chronic kidney disease of unknown source (CKDu). There have been high cases of chronic kidney disease of unknown underlying causes among the population based on hospital records. Despite the various research efforts to uncover the root cause of the disease in the area, the actual aetiology still appeared unknown. This study has reviewed all the research so far carried out regarding the disease so as to provide novel insight that will guide future research. Eleven (11) related peer-reviewed articles that focused directly or indirectly on the disease were surveyed and systematically reviewed. The findings of the relevant published articles totaling (5) were placed within the context of CKDu-related case studies particularly Sri Lankan Nephropathy and other relevant literature. The idea behind this decision is rooted from the similarity of the case as the two affected locales shared in common geography, means of livelihoods (paddy agriculture) and disease pattern. The review revealed that none of the previous investigations has drawn any scientific logical conclusion on the actual aetiology of Bade CKDu. However, previous studies have implicated exposure to heavy metals in various mediums (water and food resources) as potential 'trigger' of the disease. Therefore, it is suggested that adopting geospatially-fluent CKDu aetiology scouting approach could help to uncover the underlying cause of the disease in the area. The outcome that will emanate from adopting such type of approach will counter or confirm the existing speculations on the aetiology disease and in turn, will help concerned authorities address the issue.

Keywords: *Aetiology, Bade,CKDu, Gashua Kidney Disease, GIS, Pathogenesis, Risk factors*

INTRODUCTION

Chronic Kidney disease (CKD) has appeared to be a serious public health issue globally with varieties of known and unknown aetiologies threatening the lives of many people (Lunyera *et al*., 2016; Gashua *et al*., 2018). CKD has a highest incidence in developing countries where relatively its diagnosis and treatment are not readily available (Remuzzi and Horton, 2013). Chronic Kidney Disease of Unknown Aetiology (CKDu) has appeared in some developing countries of the world as a new form of CKD that is not related to the known traditional risk factors such as hypertension, diabetes, obesity, and frequent use and abuse of herbal and analgesic drugs (Remuzzi and Horton, 2013; Wimalawansa, 2014; Levine*et al*., 2016).

CKDu seems to be asymptomatic and only manifests at the end-stage when the kidney organs attained a stage of irretrievable damage. Chronic Kidney Disease of unknown source is a serious health issue affecting many underdeveloped countries around the world, causing high mortality and morbidity rates among population (Jayatilake, 2014). According to Levine*et al*. (2016) most of the patients affected by CKDu in less developed countries are in their active productive age of between 30-60 years in most cases. CKDu epidemic has been reported with increasing frequency around the world in areas such as parts of South East Asia (Sri Lanka), Central America, and Eastern Europe (Martin-Cleary, 2014) as well as in Africa (Abdissa, 2020).

However, apart from the identified aetiologies responsible for the disease, environmental factors such as exposure to heavy metals (Kulathunga *et al*. 2019), as well as heat stress (Jayasekara *et al*. 2019) and use of agrochemicals such as residues of glyphosate and Paraguat (Abdul *et al*., 2021) were all reported as potential risk factors. Similarly, exposure to contaminated drinking water with fluoride (Wasana *et al*., 2017; Fernando *et al*. 2020) have all been reported in the literature as drivers of CKDu. Relatively, the risk factors responsible for CKDu could be detected if thoroughly investigated (Jha *et al*., 2013). It has been reported that prolong exposure to nephrotoxic elements (Arsenic, lead, cadmium, fluoride and mercury) are the most widely recognised causers of CKDu (Wimalawansa, 2016; Kulathunga *et al*., 2019). Exposure to such toxins may occur through environmental contamination of water, food resource and occupational exposure as well, which can predispose the population to renal-related damage (Sunderland, 2010; Lunyera *et al*., 2016).

Similarly, establishing the cause-and-effect link between the suspected risk factors and CKD epidemics requires a comprehensive study. More so, the risk factors must also have a relationship with kidney damage and, has to be available in a CKDu prevalent area (Senevirathna *et al*., 2012). There must also be a source for the contamination, and the risk factor may cause a similar renal injury over the affected region (Sunderland, 2010). In line with this observation, in an attempt to investigate the cause of CKDu around the world, several studies have been conducted in many regions ranging from assessment of food resources and water using different laboratory-based approaches as reported by (Wickremasinghe *et al*., 2011; Jayasekara *et al*., 2013; Nanayakkara *et al*., 2014). Some of these studies nearly successfully discovered or identified some potential risk factors while some provided preliminary insights on the suspected factors.

Chronic kidney disease of unknown source (CKDu) is a silent deadly disease, which surreptitiously kills population as reported by Jha *et al*. (2013). With emergence of CKD, the underdeveloped countries have witnessed an increase in CKDu in the last two decades (Mills, Xu and Zhang, 2015). In Nigeria, some geographical hotspots of CKDu epidemics have emerged which similar to that of Sri Lanka (Awobusuyi *et al*., 2015). Currently, in Nigeria, the prevalence of CKD ranges from 1.60% to 12.40% as reported by Odubanjo *et al*. (2011). The sharp rise in the

incidence of End Stage of Renal Disease (ESRD) in Nigeria; particularly in Northeastern Nigeria is probably will continue if patients with CKD lack knowledge of this disease condition and its risk factors as rightly highlighted by Abdu *et al*. (2019). However, the statistics of CKD in Yobe river valley is seriously worrisome as reported by Usman, (2018) and Salamatu *et al*. (2019). The CKDu epidemics of North-eastern Nigeria specifically that of Bade community in Yobe State is similar with that of Sri Lanka Nephropathy as they shared similarity in climate and livelihoods (paddy cultivation). So also, the regions experience same pattern of CKDu epidemics as well as suspected risk factors. Therefore, this review will discuss all the preliminary investigations so far conducted that focused directly or indirectly on the disease aethology in the region. This is deemed necessary so as to present some additional recommendations that may provoke further research.

CKD IN NIGERIA: THE CASE OF NORTHERN YOBE STATE

There has been an increased mortality and morbidity due to chronic kidney disease (CKD) in Northern Yobe State, especially in Bade Local Government Area. Historical hospital records reveal that CKD is among the leading cause of mortality in the study area, especially Bade LG, as reported by Ummate *et al.* (2008). The situations have attracted the attentions of scientific research and decision makers. Several attempts have been carried in an effort to towards identifying the aetiology of the disease. For example, Waziri and Lawan, (2017) implicated drinking water and food resources produced in the area as the potential risk factors as they found concentration of heavy metals in the environment.

Gashua being the largest and most urbanized local government headquarters in the Northern Yobe, is seriously being affected with heightened cases of CKDu as indicated by the records of proximate hospitals (Ummate, 2008). It has been stated that a great percentage of CKDu patients who receives Hemodialysis in Maiduguri teaching hospital are inhabitants of Bade communities in Northern Yobe. This has led the State government to offer free dialysis in most of its tertiary hospitals in the State to reduce the economic burden of the disease in the areas as CKDu is the leading life-threatening disease among the population in the region. According Sulaiman *et al.* (2019), the disease seems to be more prevalent than in the other parts of the State or across the country. This shows that there must be something responsible for the mysterious disease outbreak in the region. Ndiath *et al*. (2014) and Friedman (2019) opined that a disease cluster or hotspot can never be emerged coincidentally and there may be a risk factors responsible. Equally, several preliminary studies had discovered high levels of cadmium and lead in the soil, water, and food resources in the region (Table 1). As reported, whether toxicity from drinking water or food resources has a role to play in the outbreak of CKDu in the area that has not yet been fully established. It is because of this, that many have speculated that environmental factors might be the root cause of the disease in the region.

REVIEW METHODS

THE STUDY AREA

Bade is a local Government Area in Yobe State, north eastern Nigeria and it is located geographically at latitude 12°52'25.12"N and longitude 11° 2'49.94"E respectively. It shares borders with Nguru Local Government Area to the north and Bursari and Jakusko to the east and west respectively. The area has an average elevation of about 370 m above sea level. The geology of the area is consistent with the general geological settings of the Lake Chad

region. The materials that made up of the geological settings of the area could be categorized basically into three: a) Crystalline Basement Complex of Pre-Cambrian age; b) sedimentary Chad Formation of Tertiary and Quaternary age; and c) alluvium and aeolian sands of Quaternary age as reported by Alkali (1995).

Bade Local Government Area is situated at the convergence of Hadeija and Jama'are rivers, and this forms Yobe River. Later the Yobe River empty into Kumadugu-Gana River at Damasak and finally join Lake Chad. This huge river system serves as the main source of water for both domestic and agricultural needs, as well as fish for most of the communities in the area. It is the presence of the river system plus the fertile loamy-clayed and silty soils that promote paddy rice cultivation in the area, a practice that serves as means of livelihood for the local population. Generally, the region is typically an agrarian zone, and the local population have predominantly engages in farming and fishing for decades due to the availability of numerous open and ground waters. Such water are sometimes found at very shallow depths, especially in the floodplains.

CLIMATE

The climate of the area is typically-tropical with clear wet and dry seasons like any other part of northern Nigeria. Recently, according to Jajere *et al*. (2021) has observed and classified three distinct seasons in the study area namely; hot-dry, warm moist and cold-dry seasons. The hot-dry season is set between April-June, while the warm-moist season begins July-September and the cold-dry season starts in December and terminates in February. The average temperature of Gashua is 43^0C, and it fluctuates from season to seasons. The area receives an average annual rainfall of 300 to 600 mm and drought mostly characterizes the rainfall. Figure 1 presents the map of the study region, the hotspot of CKDu in Yobe State, Nigeria.

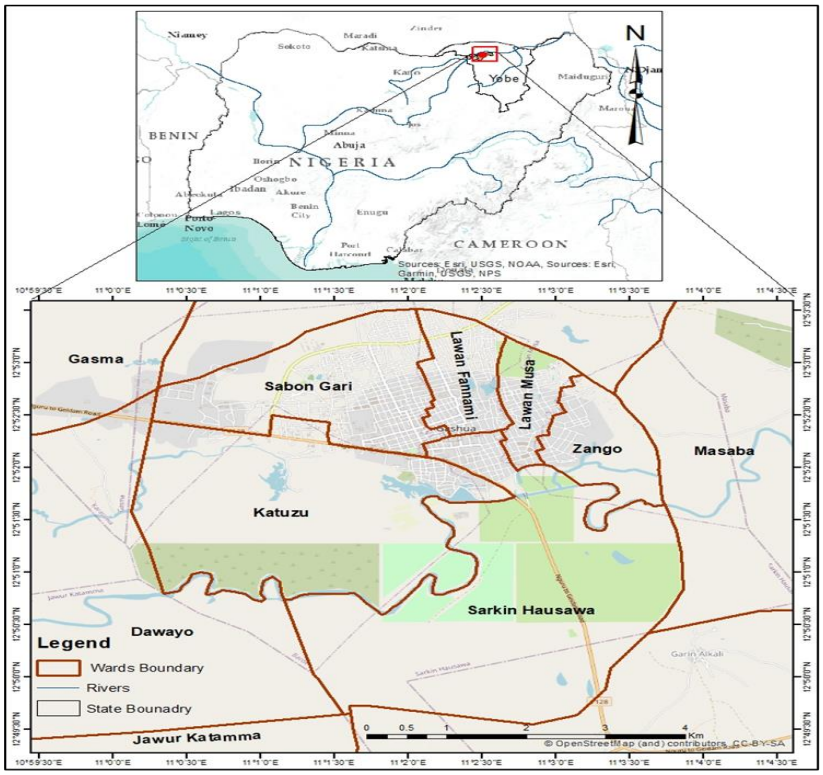

Figure 1. The location of Gashua town, the hotpot of CKDu in Northern Yobe State.

REVIEW STRATEGY

In this study, a comprehensive literature survey has been made on Chronic Kidney Disease of Bade Local Government Area, Yobe State. The keywords used in searching and surveying the published and unpublished articles via Google is 'Kidney Disease in Gashua/Bade' and 'Causes of CKDu in Nigeria/Yobe-CKDu triggers in Yobe. Eleven related articles were downloaded, the full texts of the articles were reviewed to identify the study location, study design and approaches adopted, risk factors assessed as well as their major findings. A detailed breakdown of the studies was presented in Table 1 below. After reviewing the surveyed articles, it was discovered that very few of the articles specifically focused on the disease as majority were based on suspected risk factors assessment. Out of the 11 articles, only five were directly inclined to CKD incidence in the area. As a result of this, the key findings of the reviewed articles were placed within the wider context of CKDu related case studies as well as other disease epidemics so that the missing gaps be identified. Figure 2 presents the flow chart for the review.

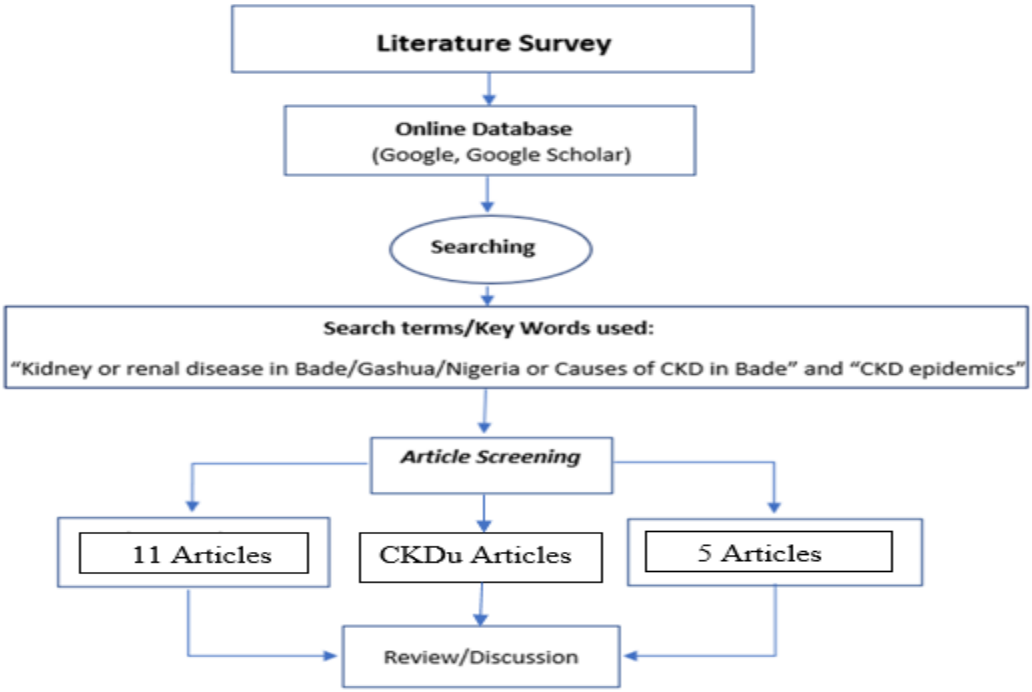

Figure 2: The Review Strategy Flow Chart

RESEARCH TO DATE

Several studies have been conducted in an attempt to investigate the risk factor(s) associated with CKDu epidemics in Gashua town and its environs. Largely, the studies were fundamentally focused on water and food resources assessment. Many specifically sought to investigate trace elements such as Cadmium, Arsenic, Mercury, lead and other elements that may play a role in CKDu epidemics as they have been contentiously debated as risk factors for CKDu in various hotspots across the world. The concentration of these elements in biological and environmental medium were quantified and assessed in the preliminary investigations as reported by the research authors (Table 1). Their findings implicated the concentration of some unsafe elements in water and food resources. However, none of the studies had scientific evidence that linked their reported risk factors with the disease occurrences.

Moreover, there are pitfalls in some of the previous studies in terms of number of samples selected and the mode of the data collection. According to Lunyera *et al.* (2016), to identify aetiology of CKDu in an identified hotspot, a

comparative site-specific risk factors investigation and population-based biomarkers screening may help to identify the disease aetiology in an identified hotspot. This technique has not been adopted particularly in the investigation of (Salamatu *et al*., 2020; Yuguda *et al.,* 2022), both studies which directly focused on the suspected CKD risk factors assessment in the study region (Yobe). This might be because of the nature of their original-research approach and goals, time constraints as well as lack of technical known-how. This is because, if different analytical approaches have been used such as geographical information systems based integrated approach, the potential risk factors for the disease would have been easily understood. Historically, disease mapping, as one of core Geographic Information System (GIS) analytics, has been recognized as essential in public health matters particularly in understanding CKDu epidemics (Vlahos *et al*., 2021). The relationship between CKDu causing factors and population characteristics could easily be investigated in CKDu hotspots in the region as local environmental factors plays an essential role in disease epidemics such as CKDu. Dayananda *et al*. (2019) for example has applied the use of GIS technology to investigate the relationship between fluoride in drinking water sources and CKDu prevalence in Sri Lanka. The summaries of the previous investigations are presented in Table 1 below.

Table 1. The Summary of the preliminary studies so far conducted in search of environmental risk factors in the study region.

	Authors	Paper title	Approach/Methods used	Findings/Results
1.	Waziri, M. and Ogugbuaja, V.O. (2010).	Inter-relationship between physicochemical water Pollution indicators: A case study of River Yobe-Nigeria.	The analyzed water samples collected and analyzed from river Yobe where human activities are mostly carried out. A total of 162 water samples were analyzed for physico-chemical parameters during dry and wet seasons.	Findings revealed a good correlation between COD/TDS, however, the correlation between BOD and TDS though was found within the acceptable range but the deviations of some points are large, indicating poor correlations between BOD and TDS.
2.	Musa, U., Waziri, M. and Hati, S.S. (2013).	Explanatory interaction profile of Cd, Pb, and Zn on the relative abundance of Fe as response variable in drinking water quality assessment.	The Study examined the quality of drinking water in three locations in N/E (Gashua, Maiduguri, Monguno). The study collected and used 96 ground water samples. Random grabbing water sampling technique were used in the analysis of the samples.	Findings revealed that Fe concentration was highest in all the sample locations except Gashua where Pb and Cd were recorded highest and this may not be good for direct human consumption.
3.	Waziri, M. and Lawan, M.M. (2017).	Incidence in lead and Cadmium in vegetables and their potential health risk to consumers in Gashua, Yobe State Nigeria.	The Study analysed the level of Cadmium (Cd) and Lead (Pb) in the vegetables grown in Gashua and the implication of possible health risks to consumers. Inductively Coupled Plasma Mass Spectrometer [ICP-MS (7500 series)] was used for the analysis.	The study found to much concentrations of Cadmium and Lead which are dangerous to potential consumers of vegetables in the region.
4.	Gashua, M. M., Kabir, J., Suleiman, M.M. and Abdulrahman H.I. (2018).	A Baseline Study for Cadmium Concentrations in Blood of Goats in Some Communities of Bade, Northern Yobe, Nigeria.	This study investigated blood samples from 356 semi-intensive ruminants from 5 randomly selected wards in the study area. Graphite Furnace Atomic Absorption-Spectrophotometry (GFAAS) was used in examining the concentration of cadmium in the bloods of sampled animals.	The study found highest concentration of Cd in the blood of sampled goats at concentrations above what Agency for Toxic Substances and Disease Registry (ATSDR) recommended.

Authors	Paper title	Approach/Methods used	Findings/Results
5. Gashua *et al*. (2018).	Assessment of some heavy metals in the liver of freshwater Catfish (Clarias gariepinus) in Northeastern Nigeria.	This study assessed the levels of Cadmium (Cd) and Lead (Pb) in the liver of freshwater catfish from three fishing sites in Bade Local Government Area along the coast of River Yobe. Atomic Absorption Spectro-photometer (AAS) was used for sample analysis.	The study discovered too much of Cd and Pb in the liver of sampled fishes in the area.
6. Oyekanmi, A., Okibe, F. and Dauda, W.P. (2018).	Toxic Elements in water and some vegetable crops in farm in Bade local government Area of Yobe State, Nigeria.	This study assessed Heavy Metals concentration in soil, water, and vegetables (lettuce, tomato, and spinach) on various farm in Bade town. These elements (As, Cd, Ni, Pb and Cr) were analysed using micro-plasma Atomic Emission Spectrophotometry (MP.AES Model 4200)	Findings established that all the Heavy Metals exceeded WHO permissible limit particularly Arsenic (As).This study is relevant since the contaminants may adversely affect human health if the produced are consumed by the locals as reported by the authors.
7. Ahmed *et al.* (2018).	Preliminary investigation of flooding problems and the occurrences of kidney disease around Hadejia-Nguru wetlands, Nigeria and the need for an Eco- hydrology solution.	This study carried out a preliminary analysis of flooding and kidney disease in the communities surrounding Hadejia-Nguru (Jigawa and Yobe State). Water quality analysis was carried out. Water samples were collected from the Hadejia and Yobe rivers.	Findings revealed too much concentration of lead (Pb), and cadmium (Cd) exceeding allowable limits. Findings recommended an Eco-hydrological system approach to identify the cause-and-effect relationship between the risk factors and the disease.
8. Sulaiman *et al*. (2019)	Chronic kidney disease of unknown origin in Northern Yobe, Nigeria: Experience from a regional tertiary hospital in Northeastern Nigeria	This study explored the prevalence of CKDu among CKD patients admitted into the renal unit of Federal Medical Centre, Nguru (FMCN). The study observed and assessed the clinical parameters of patients (such as age, sex, presence of risk factors for CKD) as well as laboratory parameters such as PCV, electrolytes, urea and creatinine, phosphate, and calcium. Glomerular filtration rate was calculated using the modification of diet in renal disease (MDRD) formula.	The study findings indicate that contribution of CKDu to the burden of CKD in Northern Yobe state is substantially high in Northern Yobe, specifically Bade and the study suspected environmental factors may likely be driver of the disease.
9. Salamatu *et al*. (2020)	Chronic Kidney Disease Associated with Consumption of Vegetables Cultivated on Contaminated Soil in Gashua, Yobe State – Nigeria	This study examined concentration of lead (Pb), chromium (Cr) and cadmium (Cd) uptake by two vegetables (onion and salad) cultivated in three contaminated areas along Gada River, Gashua.	The study reports that vegetables planted during irrigation period are polluted by Cd and Pb as found exceeded the normal limit. These heavy metals have health hazard risks and consumption of the vegetables could likely induce kidney disease.

Authors	Paper title	Approach/Methods used	Findings/Results
10. Aminu *et al.* (2021)	Comparative Study of Heavy Metals Concentration in Blood and Urine of Chronic Kidney Disease Patients and Healthy Persons in Gashua, Yobe State, Nigeria	This study compared the level of heavy metals (Pb, Cr, Cd, Ni, and Fe) in human urine and blood of healthy and Chronic kidney disease patients in Gashua using Atomic Absorption Spectroscopic Techniques (AAST)	Findings indicated too much concentration of the heavy metals in the samples (Urine and bloods) collected exceeding WHO permissible limits.
11. Yuguda *et al.* (2022).	Determination of heavy metals concentration in water, fish species and human urine associated with chronic kidney disease in Gashua, Yobe state, Nigeria.	This study analyzed the concentration of heavy metals (Arsenic, Cadmium, Copper, Chromium, and Lead) in river water samples, human Urine samples (collected from CKD case and Controls) as well as fish. Atomic Absorption Spectroscopy was used for the analysis.	The study discovered concentration of heavy metals in all samples collected. There was correlation of heavy metals concentration in CKD cases and Controls in the area. However, result was not compared with any standards benchmark recommended by any organization or authority.

DISCUSSION

THE MISSING CONTENT AND METHODOLOGICAL GAP OF THE PREVIOUS STUDIES

It should be worth observing from the review of the previous studies that most of the studies focused particularly on assessing the concentration of heavy metals such as Cd, Pb, and Zn in both drinking water and food resources (Waziri and Lawan, 2017; Gashua*et al*., 2018; Oyekanmi *et al*., 2018). While other authors such as Ahmed *et al.* (2018) focused on assessing the impact of flooding on the water quality of the surrounding river system with CKD incidences in the area. Since previous studies have implicated the concentration of nephrotoxic heavy metals in drinking water, the aetiology of the disease might be exposed to one or more of these elements. Though exposure to the trace elements and their synergic effect with other elements have not been comprehensively investigated in the region.

Therefore, it is difficult to establish the relationship between the disease occurrence and the identified risk factors or accept the reported risk factors as the 'principal trigger' of the disease in the area (Bade community). Similarly, this type of issue has been encountered when investigating the roots of CKDu in Sri Lanka as reported by (Redmon *et al*., 2014). This has provoked a series of studies in quest of finding the root of the Sri Lankan CKDu epidemics, and many of these were purely location-specific (site-specific) studies whereby the suspected risk factors of the disease were cross-examined based on the spatial prevalence of the disease.

Thus, to establish the link between CKDu incidence and the reported risk factors in Bade community, a location-specific type of study (whereby risk factors sampling will be based on the disease occurrence) needs to be carried out; the identified risk factors and the disease occurrences need to spatially investigated as distribution of risk factors and CKDu incidence may not be uniform over the area. Methodically, this could be achieved by mapping the disease mortality and morbidity, and also by classifying the area based on disease prevalence into endemic and non-endemic areas as adopted by (Jayasekara *et al*., 2013) in Sri Lanka.

It is believed that this approach will particularly help in suspected risk factor- assessment and case-control population-based investigation as the distribution of the disease incidences and the potential risk factors might not be uniform over the area. Redmon *et al.* (2014), highlighted the relevance of geography or location in CKDu's

epidemiological and aetiological investigation. This fundamental aspect has been regrettably missing in some of the preliminary studies conducted, as some randomly selected their samples without taking into account the prevalence of the disease in the area. Accordingly, Yuguda *et al*. (2022) study is the most up-to-date investigation which has nearly attempted to explore the cause-effect relationship between the disease and the suspected risk factors particularly heavy metals. This investigation used biomedical samples from CKDu cases and controls. But their approach however was limited as they did not consider hotspot-based sampling approach before taking the samples. Ideally, they should have identified and mapped the disease prevalence within the town before taking the samples cross-sectionally. This approach was demonstrated by the (Jayatilake *et al*., 2013) study where they classified and defined their study site based on the disease prevalence before cross-evaluating CKDu patient cases, controls and suspected environmental samples. Relatively, the approach was found to be logical, as it paves the way for detecting the disease aetiology easily.

To better understand the risk factors that drive CKDu in the Bade community, a geospatial technology-based approach needs to be employed in subsequent studies. Geospatial information technology, specifically Geographic Information System (GIS), is a perfect tool that can be employed in the future investigation to incorporate spatial definition in the search of the disease aetiology. The wisdom behind this is that it will allow spatial assessment of the disease aetiology in the area since the majority of the previous studies implicated environmental compounds and factors for the disease epidemics. It has been reported that the distribution of environmental nephrotoxic compounds such as cadmium and Arsenic can be influenced by various confounding factors, including local geology, as well as anthropogenic activities (Botheju *et al*., 2021). Thus, cross-mapping the disease incidence location to identify hotspots as well as surrounding area environmental factors assessment is critically crucial. According to the investigation conducted by Sommar *et al*. (2013) has found an interrelation between exposure to heavy metals such as Arsenic cadmium, lead and Chromium (popularly known as Nephrotoxins) and the development of severe renal damage in Sweden. Therefore, understanding the spatial distribution patterns of the disease together with its suspected risk factors in situ could significantly help to uncover the unknown in the area regarding the disease aetiology.

Recent studies have proven the power of GIS-based techniques in investigating disease outbreaks particularly CKD and its associated risk factors (Dissanayake *et al*., 2011; Musa *et al*., 2013; Anand *et al*., 2020). Incorporating GIS in future studies will help in the spatial visualization and modelling of the data. For example, mapping of locations with elevated trace metals concentrations and CKDu patients' distribution. Because understanding the relationship between the disease and the environmental risk factors have been the major challenge as observed in the previous investigations. Similarly, John Snow, for example, successfully used the concept of analytical mapping to study the relationship between Cholera epidemics and water points contamination in London, after several studies' failure to detect the cause of deaths in the Soho district of London in 1854 as reported by (Koch, 2014). Snow used dot maps to illustrate how incidents of cholera get clustered around a public water pump in London and this concept is now being used to trace the source of unknown disease epidemics.

Technically, the above approach, if adopted, will allow for a more comprehensive examination of the root cause of the rampant renal failure in Bade communities in Northern Yobe. In the same vein, the spatial pattern of distribution of the disease and its prevalence is are still unknown, and this is another aspect that is worth investigating to get the pathogenesis of the disease in the area. In the modern day, the techniques of spatial

epidemiology appeared to be the most promising approach used to track diseases and their associated risk factors as aptly indicated by (Graham *et al*., 2004; Stopka *et al*., 2017; Fan *et al*., 2020). This is because deploying GIS techniques could strengthen and complement the traditional research methods for CKDu particularly risk factors' data sampling as demonstrated by Rodriguez *et al*. (2014).

However, none of the previous studies reviewed has employed the aforementioned approaches; neither attempted to link their findings with biomedical samples such as human blood, and urine except the recent study of Yuguda *et al*. (2022). However, their study was not spatially defined, as they took study samples directly from hospitals. It would have been better if the CKDu cases and controls locations were mapped, and the surrounding water points and biomarkers were cross-examined for a possible relationship. Notwithstanding, the study has attempted what ought to be done to discover the aetiology of the disease in the area. It has been reported by Noble *et al*. (2014) that exposure to heavy metals could be detected in human biomedical samples such as blood, hair, and urine. Essentially, this issue of heavy metals exposure needs to be carefully examined since the local population sourced and used water from shallow boreholes and wells that are suspected to be contaminated with agrochemicals in the area. It has been highlighted in the literature that one or more of these trace elements and their synergies induces renal damage as reported by Wasana *et al*. (2017) and Botheju *et al*. (2021).

Similarly, for example, Wanigasuriya (2012) has found that the endemic CKDu hotspot in Sri Lanka overlaps with areas characterized with high groundwater fluoride content. Based on this, it is worth noting, that mere assessment of food resources and biomarkers food resources alone may not be quite sufficient to understand the aetiology of Bade CKDu incidence as viewed by the previous investigators. It is only a Geospatial-based approach that could help to accurately detect the disease aetiology in the region. As observed, the previous studies were greatly handicapped in adopting such an approach and Rodriguez *et al*. (2014) and Lunyera *et al*. (2016), as well as Sunil *et al*. (2019), have all highlighted the significance of the Geospatial based approach as it allows location-specific type of evaluation of the suspected environmental risk factors and the disease incidences. This is overly imperative since the findings of Musa *et al*. 2013; Waziri *et al*. 2017 and Oyekanmi *et al*., 2018 implicated the concentration of heavy metals (As, Pb, Fe and Cd) in water and food resources exceeding acceptable benchmarks standards and the population might have been exposed to the aforementioned chemicals.

CONCLUSION

This paper has reviewed all published contribution (peer-reviewed and grey literature) on the Chronic Kidney Disease of Unknown source (CKDu) of Bade community in Northern Yobe State. The review attempted to provide an overview of the reported studies that sought to identify the potential risk factors heightening the disease progression in the area so as to identify research gaps and equally recommend potential areas of further research. From the foregoing, it can be concluded that there are missing gaps in the investigation of the root cause of Bade CKDu. In the first place, none of the previous studies focused on the disease prevalence and its distribution patterns within the study area. Outrightly, this is supposed to be the first thing to be done before even scouting for the potential risk factors. Similarly, not all possible risk factors have been identified; and the sources of the already identified risk factors (heavy metals) have not been clearly and spatially defined. Moreover, the methodological approaches previously adopted by the authors of Bade CKDu investigation were lacking especially in the area of Geospatial technology/GIS deployment which has the capability of integrating the suspected risk factors, and the

disease prevalence as well as spatial cross-examining the factors within the affected locales. This is imperative because local geography geology and lifestyle for example could influence the distribution of CKDu risk factors in an environment. It is believed that exposure to heavy metals might be the root cause of the disease as reported in the studies reviewed but the hypothesis needs to be carefully x-rayed before drawing such a shoddy conclusion. Therefore, future research should focus on community-based or location-specific evaluation of CKDu cases, controls and spatial cross-assessment of suspected environmental factors as well as monitoring of biomarkers across the disease hotspots in the area. Applying GIS could help to locate the sources of the risk factors, as well as their spatial relationship with the disease incidences. This is essentially vital because the fundamental law of Geography enunciated by Tobler stated that 'Everything is related to everything else, but near things are more related than distant things' Thus, the outcome that will come up from the such type of study will scientifically confirm or counter the speculated claims of environmental factors as 'driver of the disease' such as groundwater heavy metals toxicity, consumption of shallow well water and food resource contamination as reported in previous research.

COMPETING INTEREST

All authors declared no any competing interests

REFERENCES

Abdissa, D. (2020). Purposeful review to identify risk factors, epidemiology, clinical features, treatment and prevention of chronic kidney disease of unknown etiology. *International Journal of Nephrology and Renovascular Disease***13**: 367.

Abdu, A., Umar, M. S. and Audi, K. Y. (2019). Knowledge and Perception of Chronic Kidney Disease in a Semi-urban Community in North-east Nigeria. *Journal of BioMedical Research and Clinical Practice* **2**(1): 25-31.

Abdul, K. S. M., De Silva, P. M. C., Ekanayake, E. M. D. V., Thakshila, W. A. K. G., Gunarathna, S. D., Gunasekara, T. D. K. S. C., Jayasinghe, S.S., Asanthi, H.B., Chandana, E.P.S. Chaminda, G.G.T., Sirobaddana, S.H. and Jayasundara, N. (2021). Occupational paraquat and glyphosate exposure may decline renal functions among rural farming communities in Sri Lanka. *International Journal of Environmental Research and Public Health* **18**(6): 3278.

Ahmed S.D., Agodzo, S.K., Adjei K.A., Deinmodel, M. and Ameso, V.C. (2018). Preliminary investigation of flooding problems and the occurrence of kidney disease around Hadeija-Nguru wetlands. Nigeria and the need for an Eco-hydrology solution. *Ecohydrology and Hydrobiology* **18**(2): 212-224.

Aminu, H.T., Uba, B. and Gadaka M. A. (2021). Comparative Study of Heavy Metals Concentration in Blood and Urine of Chronic Kidney Disease Patients and Healthy Persons in Gashua, Yobe State, Nigeria. *International Academic Journal of Applied Biomedical Sciences***2**:6: 13-20.

Awobusuyi J.O., Bakare O., Dada A., Adamu U., Abasi-Ekong U.D., Effa E., Ummate .I., Uwakwem A., Umeizudike T., Amisu A., Adekoya A., Makursidi M., Limman H.M. and Adegun P. (2015). Indices of Kidney Damage in Nigeria: A Survey of 8077 Subjects in the Six Geopolitical Zones of the Country. *Tropical Journal of Nephrology* **10**(1): 95-105.

Botheju, W. S. M., Liyanage, J. A. and Kannangara, S. D. P. (2021). The Groundwater Geochemistry and the Human Health Risk Assessment of Drinking Water in an Area with a High Prevalence of Chronic Kidney Disease of Unknown Etiology (CKDu), Sri Lanka. *Journal of Chemistry* **2021**. Article ID 1755140, 18pp. https://doi.org/10.1155/2021/1755140

Dayananda, M. D. N. R., Botheju, W. S. M., Perera, W. P. R. T. and Liyanage, J. A. (2019). Investigation of spatial distribution of fluoride in drinking water sources in CKDu prevalence areas in Sri Lanka using GIS. 4th

International Research Symposium on Pure and Applied Sciences, Faculty of Science, University of Kelaniya, Sri Lanka. 147pp.

Dissanayake, D. M., Jayasekera J.M., Adikari S.B. and Bandara, P. (2011). A Study on Geographical Distribution of Chronic Kidney Disease of Unknown Origin in Sri Lanka Using GIS and GPS Mapping. Proceedings of the Peradeniya University Research Sessions, Sri Lanka, Vol. 16, 24th November 2011, 105pp. http://dlib.pdn.ac.lk/handle/1/6414

Fan, J., Liu, X., Pan, W., Douglas, M. W. and Bao, S. (2020). Epidemiology of coronavirus disease in Gansu Province, China, 2020. *Emerging Infectious Diseases* **26**(6): 1257.

Fernando, W. B. N. T., Nanayakkara, N., Gunarathne, L. and Chandrajith, R. (2020). Serum and urine fluoride levels in populations of high environmental fluoride exposure with endemic CKDu: a case–control study from Sri Lanka. *Environmental Geochemistry and Health* **42**(5): 1497-1504.

Friedman, D. (2019). Genes and environment in chronic kidney disease hotspots. *Current Opinion in Nephrology and Hypertension* **28**(1): 87.

Fonseka, S., Jayasumana, C., Jayalath, K., Amarasinghe, M., Senanayake, K., Wijewardhane,C., Samarasinghe, D., Dahanayake, K., Mahamithawa, P. and Paranagama, P. (2012). Arsenic and hardness in ground water from chronic kidney disease of unknown etiology (CKDu) prevalent areas and non-CKDu prevalent areas in Sri Lanka. In: Ileperuma, O.A., Priyantha, N., Navaratne, A., Yatigammana, S.K. and Weragoda, S.K. (editors). Symposium Proceedings, International Symposium on Water Quality and Human Health: Challenges Ahead, March 22-23, PGIS, Peradeniya, Sri Lanka.

Gashua, M. M., Kabir, J., Suleiman, M.M. and Abdulrahman H.I. (2018). A Baseline Study for Cadmium Concentrations in Blood of Goats in Some Communities of Bade, Northern Yobe, Nigeria. *Asian Journal of Research in Animal and Veterinary Sciences***2**(2): 1-10. DOI: 10.9734/AJRAVS/2018/44244.20.

Graham, A. J., Atkinson, P. M. and Danson, F. M. (2004). Spatial analysis for epidemiology. *Acta Tropica* **91**(3): 219-225. https://dpi.org/10.1016/j.actatropica.2004.05.001

Jajere, A.A., Abbas, A.M. and Abdu, A. (2021). Rainfall Recovery in North-East Arid Zone of Nigeria: Comparative Analysis of Drought and Post Drought Decades (2021). *Asian Journal of Geographical Research* **4**(4):1–16. https://doi.org/10.9734/ajgr/2021/v4i498

Jayasekara, K. B., Kulasooriya, P. N., Wijayasiri, K. N., Rajapakse, E. D., Dulshika, D. S., Bandara, P., Fried, L.F., De Silva, A. and Albert, S. M. (2019). Relevance of heat stress and dehydration to chronic kidney disease (CKDu) in Sri Lanka. *Preventive Medicine Reports* **15**:100928. Doi:10.1016/j.pmedr.2019. 100928

Jayasekara, M.K.B., Dissanayake, D.M., Adhikari, S.B. and Bandara P. (2013). Geographical distribution of the chronic kidney disease of unknown origin in Sri lanka: in the region of irrigation reservoir. *Research International Journal of Recent Scientific Research***4** (2):107 -110.

Jayatilake, N., Mendis, S., Maheepala, P. and Mehta, F.R. (2013). Chronic kidney disease of uncertain aetiology: prevalence and causative factors in a developing country. *BMC Nephrology***14**: 180. https://doi.org/10.1186/1471-2369-14-180

Jayasinghe, S. M. M. F. (2014). Chronic kidney disease of unknown etiology should be renamed chronic agrochemical nephropathy. *MEDICC Review***16**: 72-74.

Jha, V., Garcia-Garcia, G. and Iseki, K. (2013). Chronic kidney disease: global dimension and perspectives. *Lancet***382**: 260–272.

Koch, T. (2014). 1831: The map that launched the idea of global health. *International Journal of Epidemiology* 43 (4): 1014-1020.

Kulathunga, M. R. D. L., Wijayawardena, A., Naidu, R., and Wijeratne, A. W. (2019). Chronic kidney disease of unknown aetiology in Sri Lanka and the exposure to environmental chemicals: a review of literature. *Environmental Geochemistry and Health **41***(5): 2329-2338.

Levine, K.E., Redmon, J.H., Elledge, M.F., Wanigaruriya K.P., Smith, K., Munoz, B., Waduge,V.A., Periris-John, R.J., Sathiakumar, N., Harrington, J.M., Womack, D.S. and Wickremasinghe, R. (2016). Quest to identify geochemical risk factors associated with Chronic Kidney Disease of Unknown etiology (CKDu) in an endemic region of Sri Lankan- a Multimedia laboratory analysis of biological, food and environmental samples. *Environmental Monitoring and Assessment***188**(10): 548. Doi: 10.1007/s10661-016-5524-8.

Lunyera, J., Mohottige, D., Von Isenburg, M., Jeuland, M., Patel, U.D., and Stanifer, J.W. (2016). CKD of uncertain aetiology: A Systematic review. *Clinical Journal of the American Society of Nephrology* **11**(3): 379-385.

Martin-Cleary, C. and Ortiz, A. (2014). A CKD hotspot around the world: Where, why and what the lessons are. A CKJ review series. *Clinical Kidney Journal* **7**(6): 519–523.

Mills, K.T., Xu, Y., Zhang, W., Bundy, J.D., Chen, C.S., Kelly, T.N., Chen, J. and He, J. (2015). A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. *Kidney International* **88**: 950–957. doi: 10.1038/ki.2015.230.

Musa, G. J., Chiang, P., Sylk, T., Bavley, R., Keating, W., Lakew, B., Tsou, H. and Hoven, C.W. (2013). Use of GIS mapping as a public health tool–-from cholera to cancer. *Health Services Insights* **6**: 111-118.

Musa, U., Waziri, M. and Hati, S.S. (2013). Explanatory interaction profile of Cd, Pb, and Zn on the relative abundance of Fe as response variable in drinking water quality assessment. *International Research Journal of Pure and Applied Chemistry* **3**(4):404-416.

Nanayakkara, S., Senevirathna, S. T., Abeysekera, T.,Chandrajith, R., Ratnatunga, N., Gunarathne, E. D., Yan, J., Hitomi, T., Muso, E., Komiya, T., Harada, K.H., Liu, W., Kobayashi, H., Okuda, H., Sawatari, H., Matsuda, F., Yamada, R., watanabe, T., Miyataka, H., Himeno, S. and Koizumi,A. (2014). An integrative study of the genetic, social and environmental determinants of chronic kidney disease characterized by tubulointerstitial damages in the North Central Region of Sri Lanka. *Journal of Occupational Health* **56** (1):28-38. doi: 10. 1539/joh. 13-0172-oa.

Navas-Acien A., Tellez-Plaza, M., Guallar, E., Muntner, P., Silbergeld, E., Jaar, B. and Weaver, V. (2009). Blood cadmium and lead and chronic kidney disease in US adults: a joint analysis. *American Journal of Epidemiology* **170**(9): 1156-1164.

Ndiath, M., Faye, B., Cisse, B., Ndiaye, J. L., Gomis, J. F., Dia, A. T. and Gaye, O. (2014). Identifying malaria hotspots in KeurSoce health and demographic surveillance site in context of low transmission. *Malaria Journal* **13**(1): 1-8.

Odubanjo, M. O., Oluwasola, A. O. and Kadiri, S. (2011). The epidemiology of end-stage renal disease in Nigeria: the way forward. *International Urology and Nephrology* **43**(3): 785-792.

Oyekanni, A., Okibe, F. and Dauda, W.P. (2018). Toxic Elements levels in water and some vegetables crops growth in farms in Bade Local Government Area of Yobe State, Nigeria. *Asian Journal of Physical and Chemicals Sciences* **6**(2): 1-11.

Redmon, J. H., Elledge, M. F., Womack, D. S., Wickremashinghe, R., Wanigasuriya, K. P., Peiris-John, R. J., Lunyera, J., Smith, K., Raymer, J.H. and Levine, K. E. (2014). Additional perspectives on chronic kidney disease of unknown aetiology (CKDu) in Sri Lanka–lessons learned from the WHO CKDu population prevalence study. *BMC Nephrology* **15**(1): 1-10.

Rodriguez, R. A., Hotchkiss, J. R. and O'Hare, A. M. (2013). Geographic information systems and chronic kidney disease: racial disparities, rural residence and forecasting. *Journal of Nephrology* **26**(1): 3-15.

Senevirathna, L., Abeysekara, T., Nanayakkara, S., Chandrajith, R., Ratnatunga, N., Harada, K., Hitomi, T., Komiya, T., Muso, E. and Koizumi,A. (2012). Risk factors associated with disease progression and mortality in chronic kidney disease of uncertain aetiology: a cohort study in Medawachchiya, Sri Lanka. *Environmental Health Prevention Medicine* **17**(3):191–198.

Soderland, P., lovekar, S., Weiner, D.E., Brooks, D. R. and Kaufman J. S. (2010). Chronic Kidney Disease Associated with Environmental Toxins and Exposures: Review. *Advances in Chronic Kidney Disease* **17**(3): 254-26. doi: 10.1053/j.ackd.2010.03.011.

Sommar, J. N., Svensson, M. K., Björ, B. M., Elmståhl, S. I., Hallmans, G., Lundh, T., Schon, S.M., Skerfving, S. and Bergdahl, I. A. (2013). End-stage renal disease and low level exposure to lead, cadmium and mercury; a population-based, prospective nested case-referent study in Sweden. *Environmental Health* **12**(1): 1-10. Doi: 10. 1186/1476-069X-12-9.

Stopka, T. J., Goulart, M. A., Meyers, D. J., Hutcheson, M., Barton, K., Onofrey, S., Church, D., Donahue, A. and Chui, K. K. H. (2017). Identifying and characterizing hepatitis C virus hotspots in Massachusetts: a spatial epidemiological approach. *BMC Infectious Diseases* **17**(1): 1-11. https;//doi.org/10.1186/s12879-017-2400-2

Sulaiman, M.M., Shettima, J., Ndahi, K., Abdul, H., Baba, M.M., Ummate I. and Hussein, K. (2019). Chronic kidney disease of unknown origin in Northern Yobe, Nigeria: Experience from a regional tertiary hospital in northeastern Nigeria. *Borno Medical Journal***16**(2) 1-8. DOI: 10.31173/bomj.bomj_151_16

Sunderland, P., Lovecraft, S., Weiner, D. E., Brooks, D. R. and Kaufman, J. S. (2010). Chronic kidney disease associated with environmental toxins and exposures. *Advances in Chronic Kidney Disease***17**(3): 254-264.

Ummate, I., Nwankwo, E. and Yusuf, H. (2008). The aetiology of chronic kidney disease in Maiduguri, Nigeria. *Kanem Journal of Medical Sciences***2**(2): 48-52.

Usman, S. (2018). Rising cases of chronic kidney disease in Yobe trigger concern among stakeholders. Nigeria: Accessed via https://dailypost.ng/2018/11/07/rising-cases-chronic-kidney-disease-yobe-trigger-concern-among-stakeholders/

Vlahos, P., Schensul, S. L., Anand, S., Shipley, E., Diyabalanage, S., Hu, C., Ha, Toan., Staniec, A., Haider, L., Schensul, J.J., Hewavitharane,P., Silva, T., Chandrajith, R. and Nanayakkara, N. (2021). Water sources and kidney function: investigating chronic kidney disease of unknown etiology in a prospective study. *npj Clean Water* **4**(1): 1-7.

Waller, L. A. and Carlin, B. P. (2010). Disease mapping. *Chapman & Hall/CRC Handbooks of Modern Statistical Methods*, *2010*, 217.

Wanasinghe, W.C.S., Gunarathna, M.H.J., Herath, H.M.P. and Jayasinghe G.Y. (2018). Drinking Water Quality on Chronic Kidney Disease of Unknown Aetiology (CKDu) in Ulagalla Cascade, Sri Lanka. *Sabaragamuwa University Journal* **16** (1): 17-27.

Wanigasuriya, K. (2012). Aetiological factors of chronic kidney disease in the North Central Province of Sri Lanka: a review of the evidence to-date. *Journal of the College of Community Physicians of Sri Lanka***17:** 15–20.

Wanigasuriya, K.P., Peiris,. H, Ileperuma, N., Peiris-John, R.J. and Wickremasinghe, R. (2008). Could Ochratoxin A in food commodities be the cause of chronic kidney disease in Sri Lanka? *Transactions of the Royal Society of Tropical Medicine and Hygiene* **102**: 726–726-728.

Wasana, H., Aluthpatabendi, D., Kularatne, W. M. T. D., Wijekoon, P., Weerasooriya, R. and Bandara, J. (2016). Drinking water quality and chronic kidney disease of unknown etiology (CKDu): synergic effects of fluoride, cadmium and hardness of water. *Environmental Geochemistry and Health* **38**(1): 157-168.

Wasana, H.M.S., Aluthpatabendi, D. and Bandara, J. (2012). Drinking water quality assessment towards "chronic kidney disease of unknown etiology (CKDu)" in north central province (NCP) of Sri Lanka. International Symposium on water quality and human health; challenges ahead, 22-23 March 2012. University of Peradeniya, Sri Lanka. 67pp.

Waziri, M. and Lawan, M.M. (2017). Incidence of lead and cadmium in vegetables and their potential health risks to consumers in Gashua, Yobe Nigeria. Proceedings of 65th ISERD International Conference, Mecca, Saudi Arabia, 23rd-24th January, 2017 ISBN: 978-93-86291-92-9.

Waziri, M. and Ogugbuaja, V.O. (2010). Interrelationship between physico-chemical water pollution indicators: A case study of river Yobe Nigeria. American *Journal of Scientific and Industrial Research***1**(1):76-80. http://www.scihub.org/AJSIR ISSN: 2153-649.

Wickremasinghe, A. R., Peiris-John, R. J. and Wanigasuriya, K. P. (2011). Chronic kidney disease of unknown etiology in the North Central Province of Sri Lanka: trying to unravel the mystery. *Ceylon Medical Journal***56**: 143–145.

Wimalawansa, S. J. (2016). The role of ions, heavy metals, fluoride, and agrochemicals: critical evaluation of potential aetiological factors of chronic kidney disease of multifactorial origin (CKDmfo/CKDu) and recommendations for its eradication. *Environmental Geochemistry and Health* **38**(3): 639-678.

Wimalawansa, S. J. (2019). Public health interventions for chronic diseases: cost–benefit modelizations for eradicating chronic kidney disease of multifactorial origin (CKDmfo/CKDu) from tropical countries. *Heliyon* **5**(10): e02309.

World Health Organization (WHO)(2008). Chronic Kidney Disease of Unknown Aetiology (CKDu): A New Threat to Health. Sri Lanka: WHO Country Office for Sri Lanka.

Yuguda, U., Jones, A. N., Ibrahim, U. A. and Yadima, S. G. (2022). Determination of heavy metals concentration in water, fish species and human urine associated with chronic kidney disease in Gashua, Yobe state, Nigeria. *Federal University of Wukari (FUW) Trends in Science and Technology Journal* **7**(1): 168 – 179.