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SHORT COMMUNICATION

Spatial Analysis of Chronic Kidney Disease of Unknown Aetiology (CKDu) Prevalence in Badulupura Village, Sri Lanka

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ABSTRACT

This study investigated spatial patterns of chronic kidney disease of unknown aetiology (CKDu) patients in Badulupura village. The analysis utilized published locational data for all households, including households affected by CKDu, and all wells used by CKDu-affected patients (CPA wells). The study employed Average Nearest Neighbour (ANN) and Hot Spot Analysis (Getis-Ord Gi*) tools to assess the spatial clustering of CKDu households and CPA wells. The study also explored the impact of topographical factors such as elevation, slope, and distance to watershed boundaries on the spatial distribution of CKDu patients. The ANN analysis revealed a dispersed pattern for all wells, and a random distribution for all households. However, both CKDu households and CPI wells exhibited a clustered pattern, suggesting a location-specific cause for the spatial distribution of the disease. Additionally, overlaying CKDu-affected households on the digital elevation model revealed a concentration of CKDu hot spots in high-elevation areas, while cold spots were observed in low-elevation regions. Furthermore, the t-test was employed to investigate the significance of elevation, slope, and distance to the watershed boundaries in relation to CKDu distribution. The results indicated a significant ($p<0.05$) prevalence of CKDu in high-elevation areas, while no significant association was found with slope or distance to watershed boundaries. The study revealed the presence of localized CKDu hot spots and cold spots within a small geographical area, highlighting the importance of considering topographical factors and conducting comprehensive hydrogeological and geological studies to gain valuable insights into the spatial distribution of CKDu.

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Chronic kidney disease of unknown/uncertain aetiology (CKDu) is recognized as an unresolved global non-communicable health crisis, and the causative factors remain unknown. The CKDu disease was initially reported in El Salvador and Sri Lanka in the 1990s, while it has recently been observed in other countries in Asia and Africa (Weaver *et al.,* 2015). Sri Lanka is one of the most CKDu-prevalent countries in Asia, and past research studies have revealed that the dry zone of Sri Lanka is the most CKDu-vulnerable region in the country (Abraham *et al.,* 2016; Ranasinghe *et al.,* 2019).

Recent epidemiological studies have found the existence of CKDu among certain environmental clusters based on geomorphology, geology and hydrology (Balasooriya *et al.,* 2019; Ranasinghe *et al.,* 2019; Vlahos *et al.,* 2021). In addition, many research studies have identified CKDu prevalence hot spots, geographical areas, and accurate patient locational data for epidemic regions in Sri Lanka (Balasooriya *et al.,* 2019; Jayasekara *et al.,* 2013; Ranasinghe *et al.,* 2019; Vlahos et al., 2021). Those data have significant potential to investigate spatial relationships between disease and perspective geographical contingencies by merging GIS and spatial statistical analysis techniques.

GIS software such as ArcGIS provides an array of spatial statistical tools to assess the spatial context of CKDu systematically. Anand *et al.* (2020) employed the Getis-Ord Gi* analytical tool to examine hot spots of kidney disease, and Vlahos *et al.* (2021) utilized the ArcGIS hot spot analysis tool to identify rapid CKDu progression areas.

This research attempted to assess the spatial distribution of CKDu in Badulupura village by applying spatial statistical analysis techniques. Furthermore, the spatial relationship between CKDu incidences and topography-related causal factors was investigated.

Badulupura village is located within Ginnoruwa and Wiranegama Divisions of Mahiyanganaya Divisional Secretariat Division in Badulla District, Sri Lanka (figure 1a). This village is severely affected by CKDu than other surrounding areas, with an estimated 30 % of the population affected by CKDu. Almost 98% of the population in Badulupura relies on groundwater as their primary source of drinking water, with the majority of households extracting drinking water from shallow regolith aquifers (Balasooriya *et al.,* 2019). The village covers an area of 4.9 km^2 on the right bank of the Mahaweli River. The elevation of this area ranges from 70 m to 120 m above mean sea level. The South-eastern boundary of the village borders a hilly forest area with erosion remnants around 230 m high. Most of the flat lowlands are covered with paddy fields. The residential zones are situated in the uplands and the presence of rocky outcrops and small inselbergs in this locale are noticeable characteristics.

The primary data utilized in this study consisted of georeferenced data of households and wells obtained from Balasooriya *et al.* (2019). This dataset included information on wells, which encompass all wells selected by the research team for sampling, specifically chosen based on their long-term usage within the community. These comprise wells associated with CKDu patients (CPA wells), which have been used for 5 or more years, and wells utilized exclusively by non-CKDu individuals (NCI wells) for the same period.

CKDu households comprised the residences of CKDu patients, identified through a ground survey conducted by a field team using the patients' list obtained from Girandurukotte Hospital. All households in the region were determined based on aerial images acquired through a drone survey conducted by their research team. The non-CKDu households were derived by subtracting the locations of CKDu households from all households. The spatial dataset consisted of the total of 63 wells, comprising 19 CPA wells and 44 NCI wells, along with 475 all households, including 42 CKDu households and 433 non-CKDu households. Figure 1b map illustrates the geographical distribution of all households and wells within the study area.

All geospatial data were transformed to the UTM 44N coordinate system (Universal

Transverse Mercator) to facilitate distance measurements. ArcGIS Average Nearest Neighbor (ANN) tool was used to assess the distribution patterns of CPA wells, all wells, CKDu households, and all household categories within study area of 4.91 km^2. This analysis was performed using ArcGIS 10.5 with the Geostatistical Analyst extension. The analysis involved the utilization of both Euclidean and Manhattan distances to calculate the average distance between their nearest neighbours.

The Hot Spot Analysis (Getis-Ord Gi*) tool was utilized to identify statistically significant clustering of high and low CKDu regions with respect to the distributions of all households and wells. The Hot Spot Analysis was conducted with the default distance threshold and FIXED_DISTANCE_BAND option to ensure that each feature had at least one neighbouring feature.

The detailed topographical information about the area was obtained from the Shuttle Radar Topography Mission (SRTM) 30 m digital elevation model (DEM) dataset. ArcGIS spatial analysis tools were utilized to derive slope and watershed boundaries relevant to the study area. ArcGIS Nearest tool was used to calculate nearest distance between watershed boundaries and point features in the CPA wells, all wells, CKDu households, and all household layers. The t-statistic test was used to assess the significance of slope, elevation, and proximity to watershed boundaries concerning both CKDu (CKDu households, CPA wells) and non-CKDu features (non-CKDu households, NCI wells) within the datasets of all households and wells.

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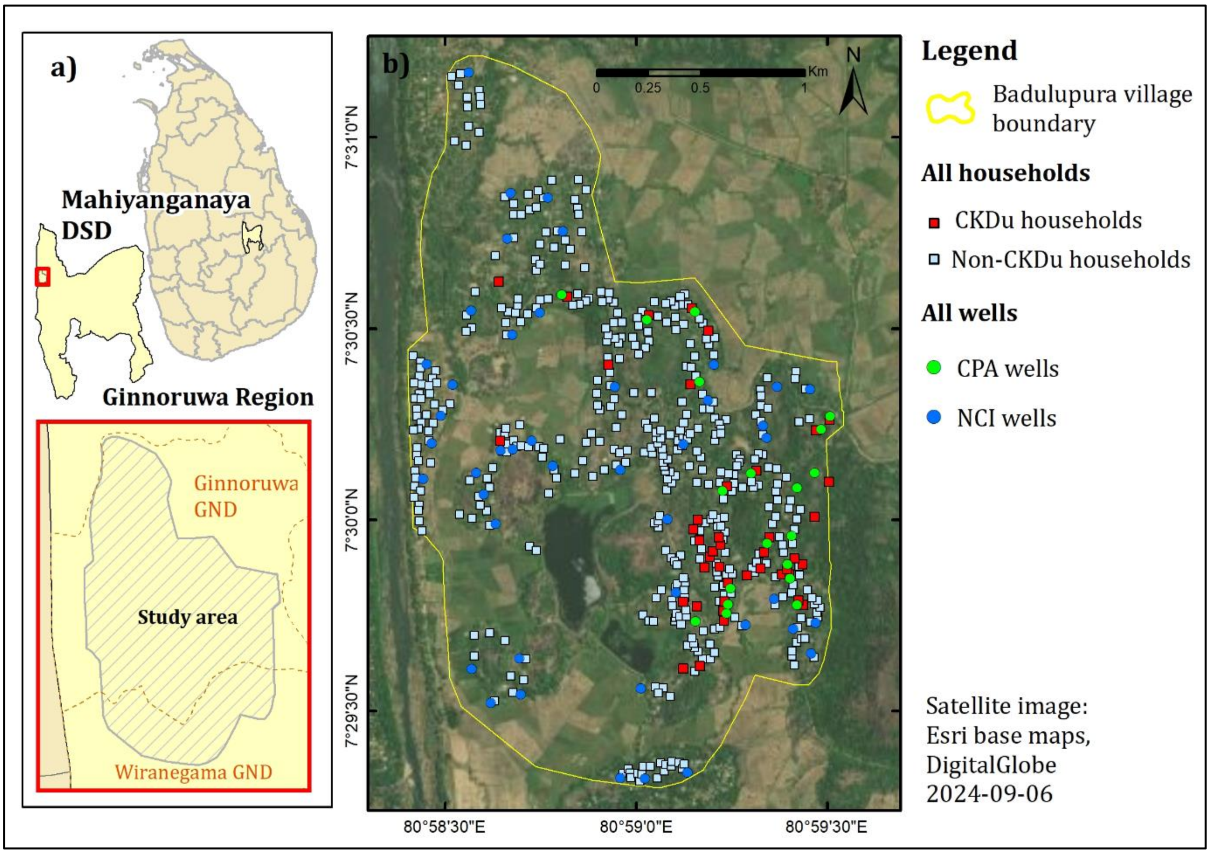

Figure 1a): Map of the study area b): An illustrative map showcases the slope gradient and the spatial distribution of all households and wells in the study area.

Table 1 displays the results of the ANN analysis for CKDu households, CPA wells, all households, and wells respective to Manhattan and Euclidean distance methods. The analysis revealed a significant clustered distribution for CKDu households and CPA wells in both distance calculation methods, with a likelihood of less than 1% and 5%, respectively by random chance. Furthermore, the analysis demonstrated a dispersed distribution pattern for all wells in relation to both distance measurement methods. Upon further examination, it was observed that households exhibited a random distribution when Euclidean distance method was used, while the Manhattan distance method revealed a clustered distribution pattern.

Table 1: Results of Average Nearest Neighbor Analysis for CKDu households, CPA wells, all households and wells.

Locations	Manhattan distance			Euclidean distance		
	Spatial distribution	Nearest Neighbour Ratio	z-score & *P* value	Spatial distribution	Nearest Neighbour Ratio	z-score & P value
CKDu households	Clustered	0.83	-2.103 *0.035*	Clustered	0.655	-4.276 *0.00*
All households	Random	0.967	-1.369 *0.172*	Clustered	0.779	-9.181 *0.00*
CPA wells	Clustered	0.704	-2.468 *0.013*	Clustered	0.573	-3.558 *0.00*
All wells	Dispersed	1.368	5.683 *0.00*	Dispersed	1.114	1.756 *0.079*

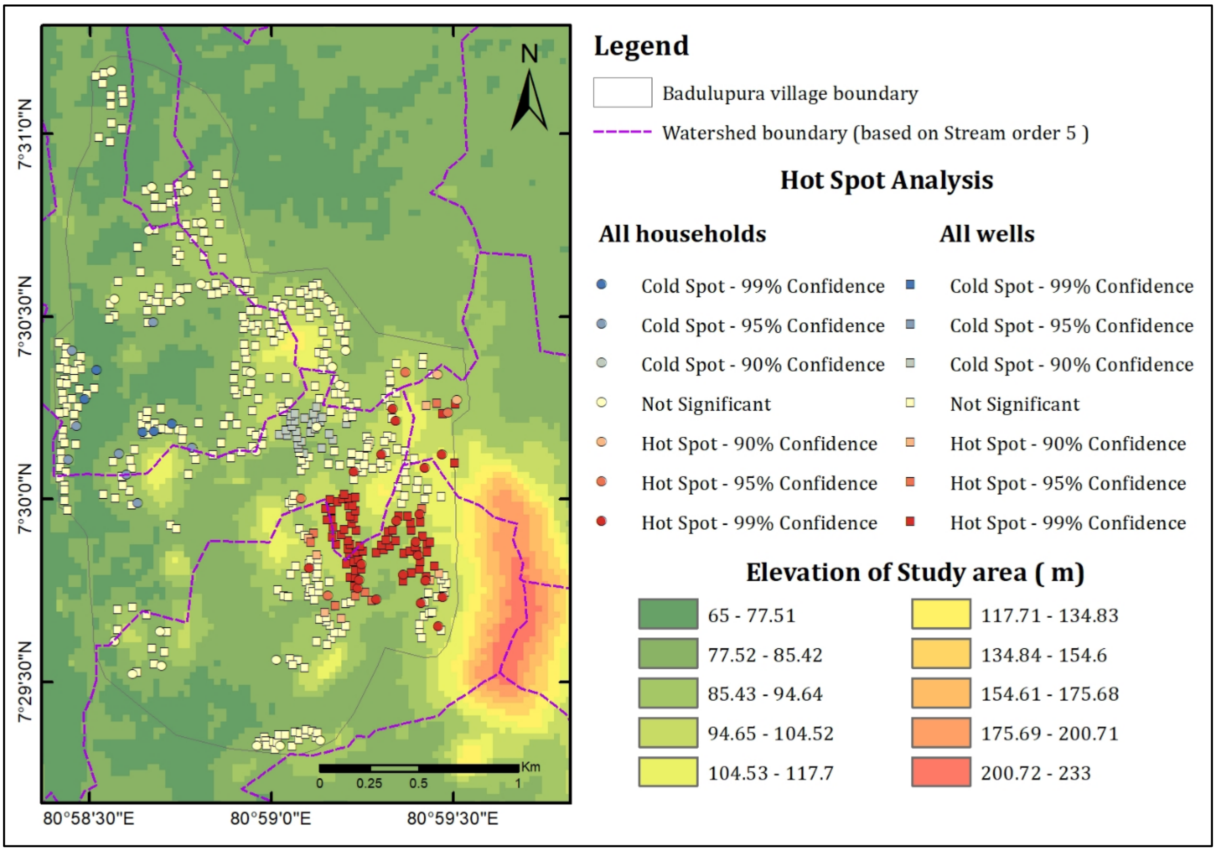

Figure 2: Hot Spot Analysis map depicting the spatial distribution of CKDu hot spots and cold spots in relation to all households and wells in the study area.

The spatial distributions of CKDu hot spots and cold spots in relation to all households and wells within the study area are depicted in the resulting Hot Spot Analysis map presented in Figure 2. When the association between wells and the digital elevation model was examined, a concentration of CKDu hot spots was observed in high-elevation areas. At the same time, cold spots were identified in low-elevation regions near the Mahaweli River bank. A similar pattern was observed for CKDu hot spots associated with all households in these elevated areas. When the distribution of CKDu hot spots and cold spots in relation to all households is examined, a clear spatial pattern is observed, with households' cold spots closely situated above the hot spots. Additionally, a discernible spatial pattern is revealed by the presence of CKDu hot spots and cold spots in both all households and wells, with CKDu hot spots and cold spots being observed on either side of the Southwest-Northeast line in the study area (see Figure 2).

The one-tail t-test results showed significant ($p<0.05$) differences in elevation between CKDu households (M = 95.3 m and SD = 36.4 m) and non-CKDu households (M = 89.4 m, SD = 50.4 m) as well as between CPA wells (M = 94.8 m, SD = 39.9 m) and NCI wells (M = 86.70 m, SD = 51.38 m, $p < 0.001$). However, no significant differences were observed in the distance to watershed boundaries between CKDu households and non-CKDu households ($p=0.36$), and between CPA wells and NCI wells ($p=0.29$). Similarly, no significant differences were found in slope between CKDu households and non-CKDu households ($p=0.33$), and between CPA wells and NCI wells ($p=0.29$).

This study investigated the distribution of CKDu households and CPA wells, which had been used by CKDu patients for 5 or more years, using the Average Nearest Neighbor analysis. The results indicated a significant clustering pattern for CKDu households and CPA wells pertaining to both the Manhattan Distance and Euclidean Distance methods, proving that CKDu is not uniformly distributed in the study area. Conversely, a dispersed spatial pattern was exhibited by the wells with respect to both distance measurement methods.

The Manhattan Distance method exhibits a higher robustness against outliers compared to the Euclidean Distance, making it well-suited for non-Euclidean spaces like geographical or urban environments. In such contexts, where distance calculations must account for obstacles or restricted movement patterns, the Manhattan Distance enables more precise measurements in complex spatial scenarios. The ANN analysis using the Manhattan Distance method revealed a random distribution pattern among all households, while the analysis using the Euclidean Distance method showed a clustered distribution pattern. Interestingly, when examining the Euclidean distance-based analysis, both all households and CKDu households, exhibited a significant clustering pattern, creating a perplexing situation. It is expected that if all households exhibit a significant clustering pattern, the CKDu households, being a subset of all households, would also display a significant clustering pattern, as they share a common area.

The Hot Spot Analysis results reveal that wells located in low elevation areas near the Mahaweli river bank were predominantly associated with cold spots, indicating a lower prevalence of CKDu cases in those regions. Conversely, CKDu hot spots were found to be concentrated in high elevation regions, indicating a higher incidence of the disease in such areas. Additionally, mean comparison provided further evidence suggesting the significant role of elevation in the distribution of CKDu cases, both in terms of households and wells, within the study region. In general, disparities arise between low and high elevation aquifers, as low elevations are prone to lower water quality from contaminants and dissolved solids, while high elevations often exhibit superior water quality and lower water tables. Nevertheless, these distinctions can vary based on regional geological and hydrological conditions. Therefore, conducting comprehensive hydrogeological studies and monitoring water quality and table levels in low and high-elevation areas is crucial to comprehend the relationship between CKDu and groundwater characteristics.

This study demonstrated the existence of localized CKDu hot spots and cold spots, even within a small geographical area. Furthermore, our hot spot analysis results aligned with the findings of Vlahos *et al.* (2021), who generated a CKDu hot spot map based on eGFR slope measurements related to the Willgamuwa region. The Hot Spot Analysis (Getis-Ord Gi*) tool can effectively identify CKDu and non-CKDu regions by utilizing CKDu-associated residential and drinking water source locations. Furthermore, this analysis enables a precise assessment of disease prevalence in specific regions.

Identifying localized CKDu hot spots and cold spots holds great significance for public health authorities and epidemiological studies in several ways. Targeted interventions can be designed to address the disease more effectively in regions at higher risk or with lower incidence. Understanding these disease clusters offers valuable insights into potential risk factors, environmental exposures, or genetic predispositions contributing to CKDu cases. Efficient resource allocation becomes possible by directing healthcare services and safe drinking water facilities to areas with high CKDu prevalence and focusing on preventive measures in areas with lower prevalence. Furthermore, the presence of localized CKDu hot spots and cold spots enables the opportunity for conducting longitudinal studies. These studies can help track changes in disease dynamics over time within these specific regions, providing valuable insights into how CKDu evolves and how risk factors may change or interact over time. Additionally, identifying these hot spots and cold spots allows for comparative analysis between CKDu high and low regions, leading to a deeper understanding of the disease's relationship to various factors.

This study conclude that the distribution of CKDu patients in Badulupura village is spatially clustered but not randomly dispersed. Further, the relationship of disease clusters with elevation revealed that associated bio-geochemical factors have a high significant influence on the distribution of the disease. These bio-geochemical factors must be further investigated mainly through hydrogeological and geological investigations.

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