European Journal of Nutrition & Food Safety
5(3): 138-149, 2015, Article no.EJNFS.2015.013
ISSN: 2347-5641

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Global Cassava Food Supply and Occurrence of Ataxic Polyneuropathy and Konzo

O. S. A. Oluwole[1*]

[1]*Neurology Unit, College of Medicine, University of Ibadan, Ibadan, Nigeria.*

Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

Article Information

DOI: 10.9734/EJNFS/2015/11453

Original Research Article

Received 17th May 2014
Accepted 18th February 2015
Published 13th March 2015

ABSTRACT

Study was done to describe global cassava food supply, and its relationship to occurrence of ataxic polyneuropathy and konzo, which are attributed to exposure to cyanide from cassava food. Cassava food supply and occurrence of ataxic polyneuropathy and konzo in all countries from 1961 to 2011, and GDP data for 2011 were analyzed. Cassava food supply ≥ 10% of expected daily calorie need was compared with GDP and occurrence of ataxic polyneuropathy and konzo. About half a billion people live where cassava food supply was ≥180 kcal/person/day. Cassava food supply ≥180 kcal/person/day was associated with GDP per capita ≤$535, p<0.0001, and with occurrence of ataxic polyneuropathy or konzo, odds ratio 30 (95% CI 7–134). Strong association of high cassava supply with low income and with endemicity of ataxic polyneuropathy and konzo indicates that reduction of contribution of cassava to energy needs will reduce the burden of disease.

Keywords: Cassava; cyanide; ataxic polyneuropathy; konzo.

**Corresponding author: Email: osaoluwole@hotmail.com;*

1. INTRODUCTION

Ataxic polyneuropathy and konzo are two neurological syndromes attributed to exposure to cyanide from cassava foods. Ataxic polyneuropathy is characterized by insidious onset sensory polyneuropathy, sensory ataxia, neurosensory deafness, and optic nerve neuropathy, which worsen progressively [1,2]. Mortality is five times higher in cases than in controls [3]. Konzo, however, is characterized by acute or subacute spastic paraparesis or quadriparesis, spastic dysarthria, visual field defects and optic atrophy [4,5]. Disability reaches maximum within hours to a few days. Visual symptoms and dysarthria often resolve leaving disabling spastic paraparesis as residual deficit [4]. Disability is not progressive, and mortality is not associated [4]. Historical reports of ataxic polyneuropathy were from Jamaica in the late nineteenth century [6] and early twentieth century [7], but it was shown to be endemic in many parts of the Caribbean in the 1960s [8]. Ataxic polyneuropathy was a subset of the epidemic of optic neuropathy and polyneuropathy which occurred in Cuba between 1991 and 1994 [9,10]. Ataxic polyneuropathy has, however, been reported from West Africa [11], East Africa [12], and Asia [13], but endemicity appears limited only to parts of Southwest and Southeast Nigeria [14], and Kerala region in South India [13]. Exposure to cyanide from unripe sugar cane [15], cigars [16], or cassava foods [1] have been associated with ataxic polyneuropathy. Konzo has been reported in endemic and epidemic forms from Congo DR [17], Mozambique [4], Tanzania [5], Central African Republic, and Eastern Cameroon [18]. Epidemics of konzo occur during droughts, when the population is exposed to cyanide from almost exclusive consumption of poorly processed cassava flour.

Cassava (Manihot esculenta Crantz) grows between latitude 30ºN and 30ºS of the equator where mean temperature is greater than 18ºC [19]. All cultivars of cassava contain two cyanogenic glycosides, linamarin [20,21] and lotaustralin [20,22]. Cassava roots are processed to products like flour, granules and pastes, from which meals are prepared [14]. Residual cyanogens often remain in cassava products due to inefficiencies of the methods of processing [23]. Although cassava foods are available in most parts of the tropics ataxic polyneuropathy and konzo are present in relatively few countries [24,14]. Presence of highly cyanogenic cassava products [25] and fresh cassava [26] in high income economies shows that exposure to cyanide from cassava is not limited to low income economies in Africa. This study was done to describe global cassava food supply, and its relationship to occurrence of ataxic polyneuropathy and konzo.

2. MATERIALS AND METHODS

2.1 Cassava Food Supply and Production and Population

List of countries and territories in the world and population data were obtained from United Nations website [27] and from rworldmap package of R Statistical Programming and Environment [28]. Countries were grouped into regions using the Global Environment Outlook GEO3 major region names. Data of cassava production in tonnes/year of all countries from 1961 to 2011 were obtained from the statistics database of the Food and Agriculture Organization of the United Nations (FAOSTAT) http://faostat3.fao.org/download/Q/QC/E, and of cassava food supply in kcal/person/day from http://faostat3.fao.org/download/FB/CC/E.

Countries were grouped into those with cassava food supply ≥180 kcal/person/day, which is approximately 10% of estimated daily calorie needs, and into those less. The gross domestic product (GDP) per capita was obtained from the World Bank database [29]. The GDP per capita of five konzo countries for 2011 were averaged as reference for low income. Cassava food supply and production during the decade 2002 to 2011 were used to assess the current supply and production status of all countries and regions.

2.2 Occurrence of Ataxic Polyneuropathy and Konzo

The PubMed database was searched to determine countries where epidemic or endemic ataxic polyneuropathy and konzo have been described. Search terms were “ataxia and polyneuropathy and cassava”, “ataxia and tropical”, “cassava and ataxia”, “cassava and motor and neuron”, “konzo”, “spastic and paraparesis and cassava”. Search was not restricted to any time period. Historical or local documents that were not indexed in PubMed were also accessed. Choropleth map was drawn to show intensities of supply of cassava foods and areas of occurrence of ataxic polyneuropathy and konzo. Cassava food supply

in kcal/person/day was grouped with reference to daily calorie needs as nil, 1-2, which is negligible, 3–18, with upper limit at 2.5% of calorie needs, 19–90, with upper limit at 5% of calorie needs, 91–180, with upper limit at 10% of calorie needs, 181–360, with upper limit at 20% of calorie needs, and > 360, which is more than 20% of calorie need per day. Cassava food supply/person/day ≥180 kcal/person/day was compared with presence or absence of ataxic polyneuropathy and konzo in all countries. Ten countries with high cassava supply, but no reports of ataxic polyneuropathy or konzo were, chosen as controls.

2.3 Statistics

Statistics were performed using appropriate packages of R Statistical Programming and Environment [28]. Descriptives were performed using the base package, odds ratios were calculated using the epicalc package, and choropleth map was produced using the rworldmap package.

3. RESULTS

3.1 Cassava Food Supply

From 2002 to 2011 cassava foods were available in 97 (43%) of 224 countries. Of these countries, 35 (36%) were in Africa, 16 (16%) in Asia, 33 (34%) in Latin America and Caribbean, 12 (13%) in Oceania, and 1 (1%) in North America. Of 24 world regions, cassava food was available in 18 (75%). Time series plots of cassava food supply in the continents from 1961 to 2011 are shown in Fig. 1a.

Geometrical mean (95% CI) cassava food supply, in the decade from 2002 to 2011, was 17 kcal/person/day (14–21) in Africa, 6 kcal/person/day (5–7) in Latin America and Caribbean, 3 kcal/person/day (2–4) in Asia, 2 kcal/person/day (1–3) in Oceania, and < 1 kcal/person/day in North America. The distribution of cassava food supply and production in world regions, and in regions where ataxic polyneuropathy and konzo had been described are shown in Table 1. Geometrical mean (range) cassava food supply was 247 kcal/person/day (232–263) in Nigeria, and 15 kcal/person/day (14–17) in India, two countries where ataxic polyneuropathy are endemic. Five countries, which had the highest supply of cassava food were Congo, Ghana, Mozambique, Angola and Liberia. Comparisons of cassava food supply in 1961 with 2011 are shown in Table 2.

Total population of countries where cassava food supply was available in any amount was 4,608,739,000; but 410,113,000 where cassava food supply was ≥180 kcal/person/day, 403,540,000 (99%) in Africa, and 6,573,000 in Latin America and Caribbean; and 92,103,000, all in Africa, where its supply was ≥360 kcal/person/day.

Cassava food supply was present in 11 countries with GDP per capita ≥$10,000, and in 5 countries with GDP per capita ≥$25,000. Using the median GDP per capita of five konzo countries, which was $535 in 2011, as reference GDP per capita was ≤$535 in 6 (32%) of 19 countries with cassava food supply ≥180 kcal/person/day compared with 7 (3%) of 205 countries with cassava food supply <180 kcal/person/day, $p<0.0001$.

3.2 Cassava Production

Time series plots of annual cassava production from 1961–2011 for the continents are shown in Fig. 1b. From 2002 to 2011 cassava was produced in 101 countries (45%) of 224. Of 101 cassava producers 36 (36%) were in Africa, 35 (34%) in Latin America and Caribbean, 13 (13%) in Asia, and 17 (17%) in Oceania. Of 24 world regions cassava was produced in 14. Log-log regression of cassava production and supply showed elasticity of 0.35, $p < 0.0001$, Fig. 2.

From 2002 to 2011 total world cassava production (tonnes) was 2,213,426,770, 1,193,444,413 (54%) in Africa, 675,312,994 (31%) in Asia, 342,416,135 (15%) in Latin America and Caribbean, and 2,253,229 (≈ 0.1%) in Oceania. The top five regional producers of cassava (tonnes) from 2002 to 2011 were Western Africa, 628,790,841, Southeast Asia, 554,177,556, South America, 328,468,948, Southern Africa, 257,149,507, and Central Africa, 200,376,738, while the top five producer countries (tonnes) were Nigeria, 416,305,885, Brazil, 249,429,076, Thailand, 223,626,495, Indonesia, 205,717,248, and DR Congo, 149,898,892. Percentage increase in cassava production in 2011 over 1961 values were 745% in Western Africa , 463% in Southeast Asia, 152% in South America, 495% Southern Africa, 201% in Central Africa.

Table 1. Global distribution of cassava food supply and production[1]

Region	Cassava	
	Supply[2] (95 % CI)	Production[3] (95 % CI)
Africa		
North	< 1	< 1
Western	71 (51–98)	173,986 (90,043–336,181)
Central	52 (32–85)	221,877 (127,026–387,554)
Eastern	10 (6–16)	4,520 (1,029–19,856)
Southern	15 (9–24)	1,540 (402–5,899)
America		
North	< 1	0
Meso	6 (5–8)	18,265 (12,749–26,168)
Caribbean	4 (3–5)	116 (65–208)
South	18 (13–26)	17,931 (6,534–49,210)
Asia		
NW Pacific and East Asia	2 (1–3)	149 (33–662)
Southeast	26 (20–33)	155,628 (63,899–379,039)
South	2 (1–3)	31 (9–107)
Central	0	0
South Pacific	2 (1–3)	113 (62–204)
Australia and New Zealand	< 2	0
Syndrome Regions		
Ataxic Polyneuropathy	77 (66–92)	480,488 (343,449–672,206)
Konzo	298 (245–364)	1,317,724 (903,400–1,922,066)
Control	182 (159–209)	450,344 (343138–591044)

[1]Data from 2002–2011 [2]Geometrical mean cassava food supply in kcal/person/day [3]Geometrical mean cassava production in tonnes/year

Geometrical mean (95% CI) annual production of cassava, in the decade between 2002–2011, was 6,519 tonnes (3,830–11,096) in Africa, 100 tonnes (54–183) in Asia, 548 tonnes (677–835) in the Americas, and 73 tonnes (42–129) in Oceania. Geometrical mean (95% CI) cassava production, in the decade between 2002–2011, in regions of the world, and regions where ataxic polyneuropathy and konzo had been described are shown in Table 1. Geometrical mean (95% CI) cassava production per capita was 60 tonnes (19–190) in 1961 but 77 tonnes (22–69) in 2011 in ataxic polyneuropathy countries, while it was 284 tonnes (160–504) in 1961, but 251 tonnes (121–522) in 2011 in konzo countries, and 144 tonnes (84–246) in 1961 and 196 tonnes (125–307) in 2011 in countries without neurological syndromes associated with exposure to cyanide from cassava foods. Cassava production per capita was 160 kg/person in 1961, but 319 kg/person in 2011 in Nigeria, while cassava food supply was 184 kcal/person/day in 1961, but 274 kcal/person/day in 2011. Comparisons of production of cassava per person in 1961 with 2011 are shown in Table 2.

3.3 Occurrence of Ataxic Polyneuropathy, Konzo, and Cassava Food Supply

Of 224 countries ataxic polyneuropathy has been reported from 8 countries, 2 as endemic and 6 as sporadic or epidemic, while konzo has been reported from 6 countries in endemic or epidemic forms. Of 210 countries without ataxic polyneuropathy or konzo, cassava food supply was ≥180 kcal/person/day in 11 (5%), but in 8 (62%) of 13 countries with ataxic polyneuropathy or konzo, odds ratio 30 (95% CI 7–134). Ten countries with high cassava food supply, but no report of ataxic polyneuropathy or konzo, were Ghana, Benin, Togo, Paraguay, Madagascar, Uganda, Guinea, Zambia, Rwanda, and Gabon. Time series plots of cassava production and food supply in ataxic polyneuropathy, konzo, and control countries are shown in Fig. 3. Fig. 4 shows the choropleth map of intensity of cassava food supply and occurrence of neurological syndromes.

Table 2. Changes in per capita cassava food supply and production

Region	Cassava supply[1] (95 % CI)		Cassava production[2] (95 % CI)	
	1961	2011	1961	2011
Africa				
North	0	< 1	< 1	< 1
Western	72 (23–228)	68 (21–220)	35,405 (2,811–445,878)	194,363 (18,250–2,069,908)
Central	60 (7–502)	51 (8–333)	98,167 (11,034–873,319)	217,683 (21195–2,235,746)
Eastern	21 (1–310)	10 (1–81)	26,523 (114–6,191,545)	49,668 (12–1,950,862)
Southern	14 (2–87)	15 (2–92)	670 (8–53,768)	1,726 (12–253,756)
America				
North	< 1	< 1	0	0
Meso	7 (2–19)	7 (3–16)	3,628 (217–60,656)	19,641 (4,144–93,091)
Caribbean	4 (2–9)	5 (2–9)	107 (14–799)	109 (98–121)
South	21 (6–75)	17 (5–52)	6,297 (135–293,890)	15,137 (398–575,411)
Asia				
NW Pacific[3]	2 (1–4)	2 (1–4)	149 (46–48,828)	152 (38–60,087)
Southeast	13 (4–45)	28 (11–72)	62,071 (8,419–457,642)	232,183 (7,661–7,036,980)
South	2 (1–7)	2 (1–7)	20 (0–2,031)	28 (0–3,416)
Central	0	0	0	0
South Pacific	3 (1–9)	2 (1–4)	153 (17–1,385)	105 (105 (14–794))
Australia[4]	0	< 1	0	0
Syndrome Areas				
AP[5]	130 (41–410)	120 (44–331)	528,273 (127,697–2,185,432)	2,230,792 (475,496–10,465,780)
Konzo	666 (342–1,297)	401 (216–744)	1,105,370 (496,646–2,460,191)	3,614,194 (1,043,327–12,519,949)
Controls	298 (201–432)	400 (246–400)	405,713 (214,190–768,491)	2,101,518 (959,947–4,600,644)

[1]Geometrical mean cassava food supply in kcal/person/day, [2] Geometrical mean cassava production in tonnes/year, [3]North West Pacific and East Asia, [4]Australia and New Zealand, [5]Ataxic polyneuropathy

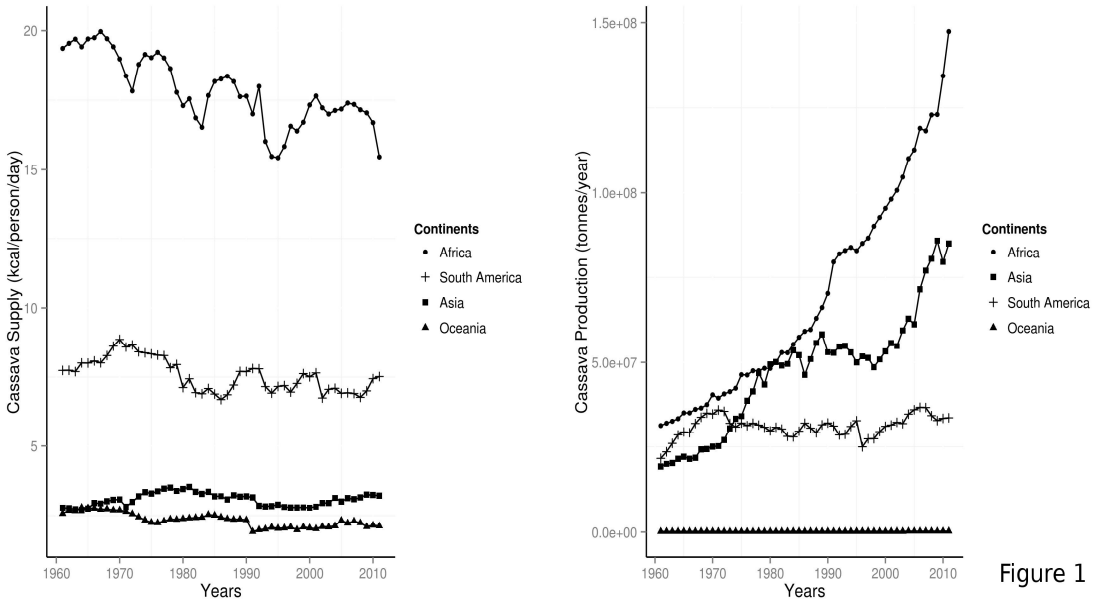

Fig. 1. Time series plots of cassava supply and production in continents

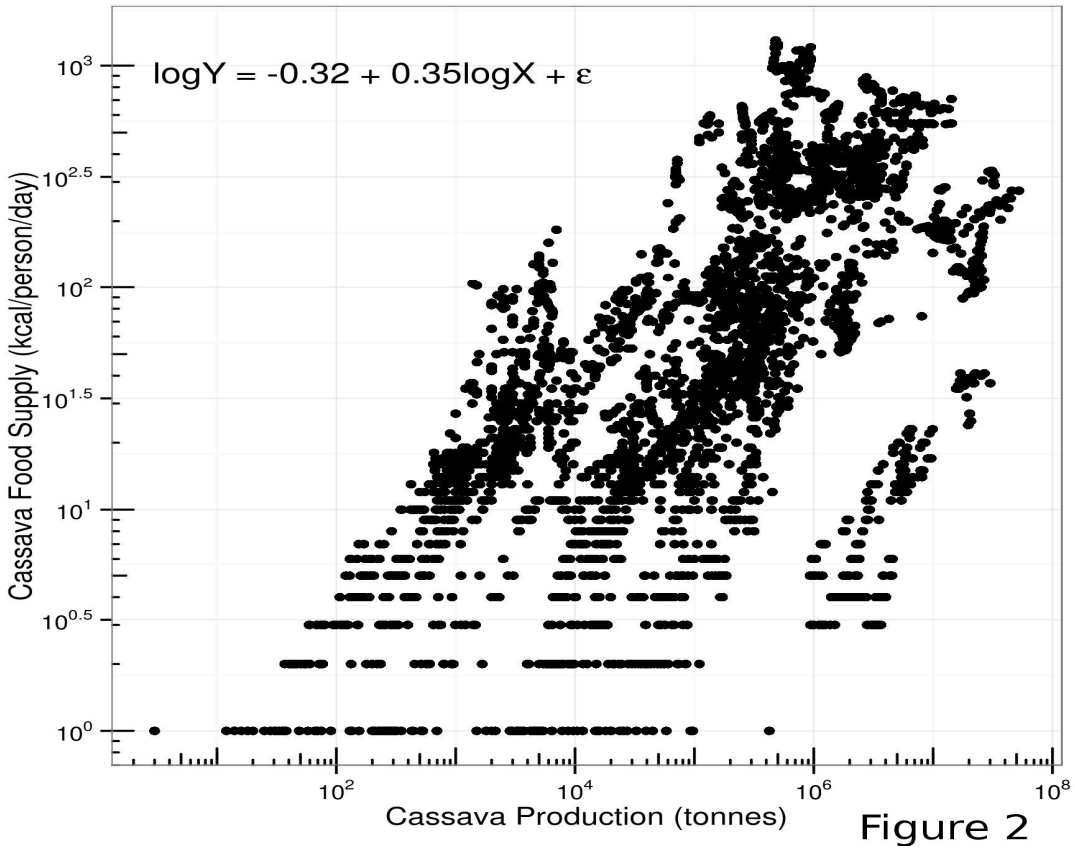

Fig. 2. Log-log plot of cassava supply and production

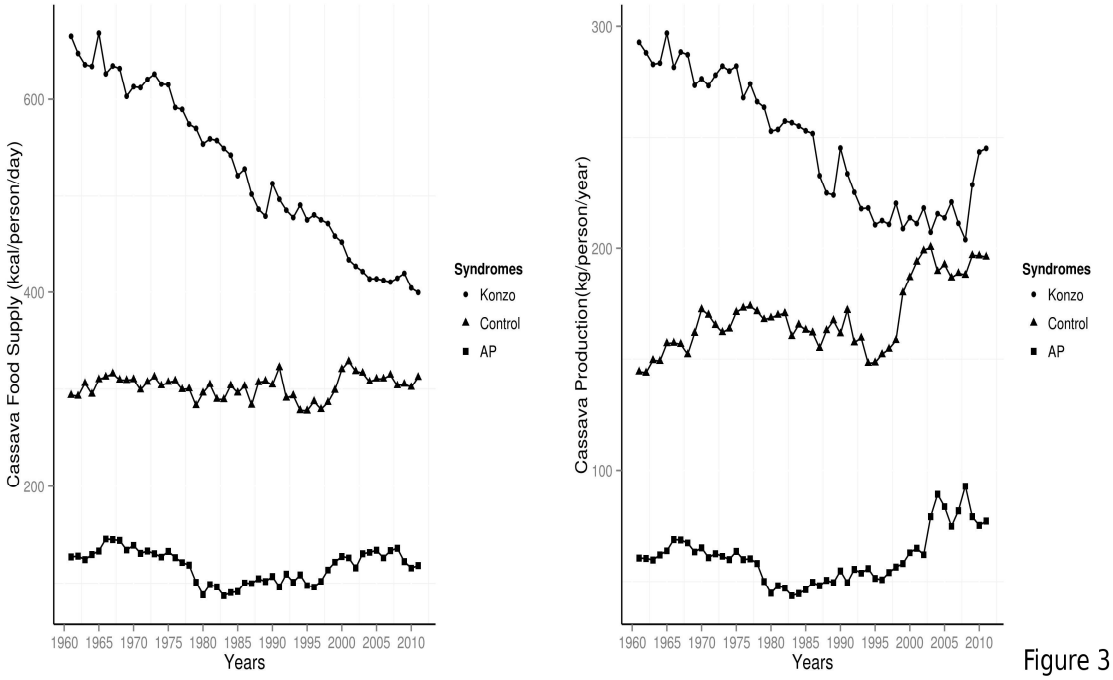

Fig. 3. Time series plots of cassava supply and production in regions of endemicity and controls (AP is ataxic polyneuropathy)

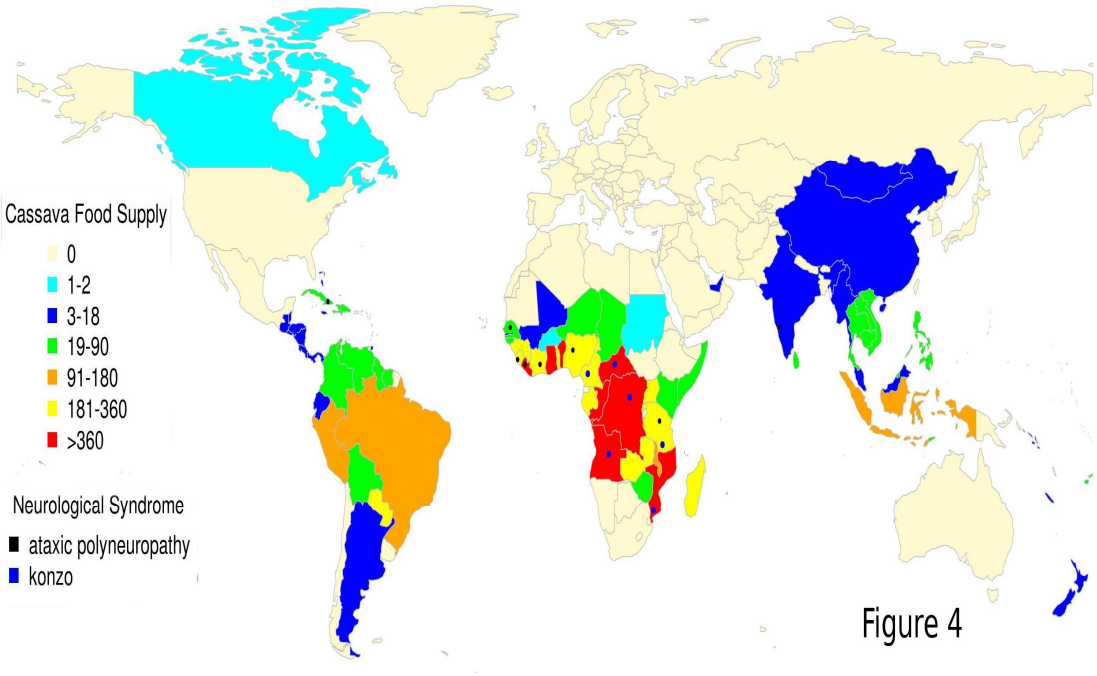

Fig. 4. Choropleth world map of cassava supply and areas of occurrence of ataxic polyneuropathy and konzo (Cassava food supply in kcal/person/day)

4. DISCUSSION

This study shows that cassava foods are available in high and low income countries, but they contribute significantly to energy needs only in low income countries, which are mostly in Africa. The low GDP of konzo countries, an average of $535, indicates that these countries are among the poorest in the world. Since cassava is a source of cheaper calories than other major crops [30], the strong statistical association of low GDP per capita and high cassava food supply, in this study, indicates that low income is the reason why this cheap energy source dominate the diet of very poor tropical countries. The population of all countries where cassava food is available in any amount, which is over 4 billion, shows that the potential distribution of cassava foods is large, but since only half a billion people live in countries where cassava food supply is ≥10% of calorie needs and about one hundred and fifty million where it is ≥ 20% of calorie needs, much less people are at risk of exposure to cyanide from cassava foods. Market surveys, which showed very high levels of cyanogens in cassava snacks in Australia [25] and in fresh cassava roots in Denmark [26], indicate that exposure to cyanide from cassava food is a potential public health problem in high income economies, but the number of exposed is insignificant compared with African countries, where more than 99% of potentially exposed people live. Thus, the risk of exposure to cyanide from cassava food is confined largely to African countries.

Although cassava is produced in 14 of 24 world regions, the major regional producers are Western Africa, Southeast Asia, South America, Southern Africa and Central Africa. Since more than 50% of the world's total from 2002–2011 was produced in Africa, this continent is the leading producer. Absence of significant difference between total cassava produced in 1961 and 2011 in all regions of production indicates that production is not declining in any of the world regions (Table 2), although increase production is seven fold in Western Africa, and four fold in Asia and South America. While cassava production in Africa, Asia, and South America were similar in 1961, the trends increased markedly in Africa and Asia, but not in South America. These differences may be partly due to the impact of climate changes, which favor cassava production in some regions, or to increase production of cassava for ethanol and other uses.

Intense production of cassava has been observed in the endemic areas of ataxic polyneuropathy in Nigeria [31] and Kerala, India [30], and in konzo affected countries [32,33]. In this study the finding of higher production of cassava in ataxic polyneuropathy countries, both sporadic and endemic, and in konzo countries than the African continent average supports this observation. The log-log plot of cassava production and cassava food supply suggests that an economic model will describe the relationship, Fig. 2. Although the log-log plot is not demand and supply relationship, the elasticity of 0.4 shows that for 10% increase in cassava production, there is corresponding 4% increase in supply of cassava products. This relationship probably holds strongly in areas of high production where endemic ataxic polyneuropathy and konzo occur. Although the trends of total cassava production increased from 1961–2011 in all the continents, Fig. 1, decline of per capita production from 1961 to the mid-1990s in konzo affected countries, Fig. 3, indicates that production did not match population growth in these areas. Regional variations in food crop productions have been linked to climate change, which has increased productivity in some regions, but had decreased it in others. Central and Southern Africa, which has been shown to suffer the negative consequences of climate change [34], is the area where seasonal epidemics of konzo occur during droughts. Thus, climate change and its effects on food productivity may play a role in low agricultural productivity and endemicity of konzo.

Cassava, *Manihot esculenta* Crantz, and other major food crops like rice, *Oryza spp.*, maize, *Zea spp.*, sugar cane, *Saccharum spp.*, millet, *Paspalum spp.*, oats, *Avena spp.*, and wheat, *Triticum spp.* [35,36] are cyanogenic during development [20,22] but only the mature edible roots of cassava are cyanogenic [37,38]. Although cassava is usually processed extensively before consumption, experimental [39,40] and field studies [41,42] have shown that cassava foods cause exposure to cyanide. The sources of cyanide are the cyanohydrin and unhydrolyzed cyanogens, which remain in cassava foods due to inefficiencies of the methods of processing [14,43]. Methods of processing cassava roots to pastes, which require soaking cassava roots in water until the tissues disintegrate, reduce the concentrations of cyanogens much more effectively [43] than methods that process cassava to flour using sun-drying [33,44]. Shortage of water in konzo

communities has been proposed as the reason while the sun-drying method is practised [45]. While cassava flour is the dominant cassava food in endemic konzo communities, *gari*, a granular product from cassava, is dominant in endemic ataxic polyneuropathy communities in Nigeria. The concentrations of cyanogens in *gari*, which is significantly higher in markets of endemic than those of non-endemic areas in Nigeria [14], have been shown to be dependent on the method of processing [23]. Culinary reasons rather than lack of water have, however, been found to explain the choice of processing method in the endemic ataxic polyneuropathy communities [31]. Thus, high concentrations of cyanogens are present in cassava foods in endemic ataxic polyneuropathy and konzo communities.

Studies of the 1960s showed that cassava contributed more than 70% of daily calorie needs in the endemic communities in Southwest Nigeria [1,46], while in the 1970s the contribution of cassava to daily energy needs in Kerala, India was 700 kcal/person/day, more than 40 times the national average [30]. Studies in the 2000s showed that consumption of cassava food in the endemic communities of Southwest Nigeria [14] and Kerala India [13] remained high. In the endemic communities of Southwest Nigeria, consumption of cassava food two or more times daily by more than 80% of the population, indicates that cassava supplies more than 1,000 kcal/person/day for most of the population [47]. Consumption in konzo endemic communities is also much higher than non-endemic communities [48]. In this study ataxic polyneuropathy or konzo have been reported in sporadic, endemic, or epidemic form from each of the top five regional producers of cassava. Cassava food supply in konzo countries, which is almost 20 times the African continent average in this study, and the reports of high consumption in endemic areas of ataxic polyneuropathy show the high intensity of cassava consumption in the endemic areas. Thus, high cassava food supply is present in all areas where ataxic polyneuropathy or konzo have been described.

The causation of ataxic polyneuropathy and konzo remain unproven although exposure to cyanide is the most consistent risk factor that have been identified. Case series studies of institutionalised subjects in the 1960s [49,50] showed that a subset of them with ataxic polyneuropathy improved on vitamin B treatment. Subjects with endemic ataxic polyneuropathy do not, however, live in extreme poverty or in areas of food shortages. Deficiency of thiamine [51], vitamin B [52], and riboflavin [53] are also considered causal factors for ataxic polyneuropathy. Subjects with ataxic polyneuropathy and control subjects in Nigeria [54] and Cuba [55], however, had similar levels of thiamine. Clinical trials of vitamin B [52], riboflavine [53], and riboflavine and cystine [56] were unsuccessful in Nigerian subjects. Thus, it appears endemic or epidemic ataxic polyneuropathy are not caused by vitamin deficiencies.

The strong association of occurrence of ataxic polyneuropathy and konzo with high cassava supply in this study supports the putative role of exposure to cyanide and causation of these two neurological syndromes. While the absence of these syndromes in some areas of high cassava food supply, and case control studies in Nigeria [42], Mozambique [4], and Tanzania [5], which did not show association, have questioned the aetiological role of cyanide exposure, the consistent findings of high residual cyanogens in cassava foods in endemic areas of konzo and ataxic polyneuropathy [14,57] make it difficult to reject the cyanide hypothesis. It is noteworthy that the putative risk factor is not consumption of high quantities of cassava foods, but of foods with high residual cyanogens [14,47]. Thus, why the putative role of cyanide in the causation of endemic ataxic polyneuropathy and konzo remain unconfirmed after more than 50 years of research ecological studies continue to show high gradient of exposure to cyanide between endemic and non-endemic areas.

The major limitation of this study is the historical rather than active concurrent collection of food supply and occurrence data. Further, country level data often underestimates actual food consumed. This is illustrated by consumption of cassava foods in countries in Europe [26], which is not shown in the FAO database. Nonetheless, since recent publications have shown persistent occurrence of ataxic polyneuropathy and konzo in the endemic areas the application of this study design is valid. For global analysis of this nature, however, actual data collection will be a difficult major undertaking.

5. CONCLUSIONS

This study shows that cassava food supply is not restricted to low income economies, but very high supply is strongly associated with low GDP.

Elasticity of 0.4 shows that economic factors contribute to the relationship of cassava production and its food supply. Strong association of high cassava food supply and occurrence of ataxic polyneuropathy and konzo indicate that the burden of disease will be reduced by reducing the contribution of cassava foods to total calorie needs. Although supply of fresh cassava roots and its food products to high income economies has raised public health concerns, the affected population is much smaller than in Africa.

FINANCIAL SUPPORT

This research received no grant from any funding agency in the public, commercial or not for profit sectors. No personal or financial relationship that may influence or bias the content exists.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. Osuntokun BO. An ataxic neuropathy in Nigeria: a clinical, biochemical and electrophysiological study. Brain. 1968; 91:215–248.
2. Oluwole OSA, Onabolu AO, Link H, Rosling A. Persistence of tropical ataxic neuropathy in a Nigerian community. J Neurol Neurosurg Psychiatry. 2000;69:96–101.
3. Oluwole OSA, Onabolu AO. High mortality of subjects with endemic ataxic polyneuropathy in Nigeria. Acta Neurol Scand. 2004;110:94–99.
4. Ministry of Health Mozambique. Mantakassa: an epidemic of spastic paraparesis associated with chronic cyanide intoxication in a cassava staple area in Mozambique. 1. Epidemiology and clinical and laboratory findings in patients. Bull World Health Organ. 1984;62:477–484.
5. Howlett WP, Brubaker GR, Mlingi N, Rosling H. Konzo, an epidemic upper motor neuron disease studied in Tanzania. Brain. 1990;113:223–35.
6. Strachan H. On a form of multiple neuritis prevalent in the West Indies. Practitioner. 1897;59:477–484.
7. Scott HH. An investigation into an acute outbreak of 'central neuritis'. Ann Trop Med Parasitol. 1918;12:109–196.
8. Montgomery RD, Cruickshank EK, Robertson WD, McMenemey WH. Clinical and Pathological Observations on Jamaican Neuropathy. Brain. 1964;87: 425–462.
9. Ordunez-Garcia PO, Nieto FJ, Espinosa-Brito AD, Caballero B. Cuban epidemic neuropathy, 1991 to 1994: History Repeats Itself a Century after the "Amblyopia of the Blockade". Am J Public Health. 1996;86:735–743.
10. Hedges RD, Hirano M, Tucker K, Caballero B. Epidemic Optic and Peripheral Neuropathy in Cuba: A unique Geopolitical Public Health Problem. Surv Ophthalmol. 1997;41:341–353.
11. Njor J. Tropical Ataxic Neuropathy in Liberians. Trop Geogr Med. 1990;42:92–94.
12. Plant GT, Mtanda AT, Arden GB, Johnson GJ. An epidemic of optic neuropathy in Tanzania: characterisation of the visual disorder and associated peripheral neuropathy. J Neurol Sci. 1997;145:127–40.
13. Madhusudanan M, Menon MK, Ummer K, Radhakrishnanan K. Clinical and etiological profile of tropical ataxic neuropathy in Kerala, South India. Eur Neurol. 2008;60:21–26.
14. Oluwole OSA. Endemic ataxic polyneuropathy in Nigeria. PhD thesis. Stockholm: Karolinska Institutet, 2002;71.
15. Roman GC, Spencer PS, Schoenberg BS. Tropical myeloneuropathies: the hidden endemias. Neurology. 1985;35.8:1158–70.
16. The Cuba Neuropathy Field Investigation Team. Epidemic optic neuropathy in Cuba–clinical characterization and risk factors. N Engl J Med. 1995;333:1176–82.
17. Diasolua Ngudi D, Banea-Mayambu JP, Lambein F, Kolsteren P. Konzo and dietary pattern in cassava-consuming populations of Popokabaka, Democratic Republic of Congo. Food Chem Toxicol. 2011;49:613–9.
18. Ciglenecki I, Eyema R, Kabanda C, Taafo F, Mekaoui H, Urbaniak V. Konzo outbreak among refugees from Central African Republic in Eastern region, Cameroon. Food Chem Toxicol. 2011;49:579–82.
19. Nassar NAM, Hashimoto DYC, Fernandes SDC. Wild Manihot species: botanical aspects, geographic distribution and economic value. Genet Mol Res. 2008;7:16–28.

20. Nartey F. Studies on cassava. Manihot utilissima Pohl-I. Cyanogenesis: The biosynthesis of linamarin and lotaustralin in etiolated seedlings. Phytochemistry. 1968;7:1307–1312.
21. Clapp RC, Bissett FH, Coburn RA, Long L. Cyanogenesis in Manioc: Linamarin and Isolinamarin. Phytochemistry. 1966;5: 1323-1326.
22. Du L, Bokanga M, Moller BL, Halkier BA. The Biosynthesis of Cyanogenic Glucosides in Roots of Cassava. Phytochemistry. 1995;39:323–326.
23. Oluwole OSA, Onabolu AO, Cotgreave IA, Rosling H, Persson A, Link H. Low prevalence of ataxic polyneuropathy in a community with high exposure to cyanide from cassava foods. J Neurol. 2002;249:1034–1040.
24. Tylleskär T. The Causation of Konzo: Studies on a Paralytic Disease in Africa. PhD thesis. Uppsala University, 1994.
25. Miles D, Jansson B, Maia MC, et al. A survey of total hydrocyanic acid content in ready-to-eat cassava-based chips obtained in the Australian market in 2008. J Food Prot. 2011;74:980–985.
26. Kolind-Hansen L, Brimer. The retail market for fresh cassava root tubers in the European Union (EU): the case of Copenhagen, Denmark - a chemical food safety issue? J Sci Food Agric. 2009;90:252–256.
27. United Nations. United Nations Populations Statistics; 2013. Available: http://www.un.org/.
28. R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing. Vienna, Austria; 2014.
29. Bank World. Gross Domestic Product. Ed. by Windows Phone Central; 2013. Available:http://data.worldbank.org/indicator/NY.GDP.PCAP.CD.
30. Cock JH. Cassava: a basic energy source in the tropics. Science. 1982;218:755–762.
31. Oluwole OSA. Cyanogenicity of cassava varieties and risk of exposure to cyanide from cassava food in Nigerian communities. J Sci Food Agric. 2008;88:962–969.
32. Nambisan B. Evaluation of the effect of various processing techniques on cyanogen content reduction in cassava. Acta Horticulturae. 1994;375: 193–201.
33. Banea M, Tylleskr T, Rosling H. Konzo and Ebola in Zaire. Lancet. 1997;349:621.
34. Trenberth KE, Jones PD, Ambenje P, et al. Observations: surface and atmospheric climate change. In: Climate Change 2007: The Physical Science Basis. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change. Ed. by Solomon S, Qin D, Manning M, et al. Cambridge University PrCam, Cambridge, UK. 2007; 273–313.
35. Clark A. Report on the effects of certain poisons contained in food -Plants of West Africa upon the health of the native races. J Trop Med Hyg. 1936;39:269–276.
36. Honig DH, Hockridge ME, Gould RM, Rackis JJ. Determination of cyanide in soybeans and soybean products. J Agric Food Chem. 1983;31:272–275.
37. Jones DA. Why are so many food plants cyanogenic? Phytochemistry. 1998; 47:155–161.
38. Montgomery RD. The medical significance of cyanogen in plant foodstuffs. Am J Clin Nutr. 1965;17:103–113.
39. Hernandez T, Lundquist P, Oliveira L, Perez Cristia R, Rodriguez E, Rosling H. Fate in humans of dietary intake of cyanogenic glycosides from roots of sweet cassava consumed in Cuba. Nat Toxins. 1995;3:114–7.
40. Oluwole OSA, Onabolu AO, Sowunmi A. Exposure to cyanide following a meal of cassava food. Toxicol Lett. 2002;135:19-23.
41. Monekosso GL, Wilson J. Plasma thiocyanate and vitamin B12 in Nigerian patients with degenerative neurological disease. Lancet. 1966;1:1062–1064.
42. Oluwole OSA, Onabolu AO, Cotgreave IA, Rosling H, Persson A, Link H. Incidence of endemic ataxic polyneuropathy and its relation to exposure to cyanide in a Nigerian community. J Neurol Neurosurg Psychiatry. 2003;74:1417–1422.
43. Agbor-Egbe T, Lape MI. The effects of processing techniques in reducing cyanogen levels during the production of some Cameroonian cassava foods. J Food Compost Anal. 2006;19:354–363.
44. Ernesto M, Cardoso AP, Nicala D, et al. Persistent konzo and cyanogen toxicity from cassava in northern Mozambique. Acta Trop. 2002;82:357–362.
45. Nzwalo H. The role of thiamine deficiency in konzo. J Neurol Sci. 2011;302(1-2):129–131.
46. Monekosso GL, Annan WGT. Clinical

epidemiological observations on an ataxic syndrome in western Nigeria. Trop Geogr Med. 1964;4:316–323.
47. Oluwole OSA, Oludiran AO. Geospatial association of endemicity of ataxic polyneuropathy and highly cyanogenic cassava cultivars. International Journal of Health Geographics. 2013;12:41.
48. Cliff J, Muquingue H, Nhassico D, Nzwalo H, Bradbury JH. Konzo and continuing cyanide intoxication from cassava in Mozambique. Food Chem Toxicol. 2011;49.3:631–5.
49. Latham MC. Nutritional aetiology of a neuropathy found in Tanganyika. Brt. J. Nutr. 1964;18:129–134.
50. Haddock DRW, Ebrahim GJ, Kapur BB. Ataxic neurological syndrome found in Tanganyika. BMJ. 1962;2:1442–1443.
51. Adamolekun Bola. Neurological disorders associated with cassava diet: a review of putative etiological mechanisms. Metab Brain Dis. 2011;26:79–85.
52. Monekosso GL, Annan WGT, Ashby PH. Therapeutic effect of vitamin B complex on an ataxic syndrome in western Nigeria. Trans R Soc Trop Med Hyg. 1964;58:432–436.
53. Osuntokun BO, Langman MJ, Wilson J, Aladetoyinbo A. Controlled trial of hydroxocobalamin and riboflavine in Nigerian ataxic neuropathy. J Neurol Neurosurg Psychiatry. 1970;33:663–6.
54. Osuntokun BO, Aladetoyinbo A, Bademosi O. Vitamin B nutrition in the Nigerian tropical ataxic neuropathy. J Neurol Neurosurg Psychiatry. 1985;48:154–6.
55. Macias-Matos C, Rodriguez-Ojea A, Chi N, Jimenez S, Zulueta D, Bates CJ. Biochemical evidence of thiamine depletion during the Cuban neuropathy epidemic, 1992-1993. Am J Clin Nutr. 1996;64:347–353.
56. Osuntokun BO, Langman MJ, Wilson J, Adeuja AO, Aladetoyinbo. Controlled trial of combinations of hydroxocobalamin-cystine and riboflavine-cystine, in Nigerian ataxic neuropathy. J Neurol Neurosurg Psychiatry. 1974;37:102–4.
57. Banea M. Dietary exposure to cyanogens from cassava. PhD thesis. Uppsala: Uppsala University; 1997.

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