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Review Article

Pellagra in South Africa from 1897 to 2019: a scoping review

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Abstract

Objective: Pellagra is a nutritional deficiency disease associated with niacin (vitamin B_3) deficiency. The history of pellagra is well documented for Europe and the USA, but less is known about the prevalence in sub-Saharan African countries. This study documents the history of pellagra in South Africa, as diagnosed based on dermatological symptoms.
Design: Scoping review of information from scientific databases, library archives, other archives and record services and from Statistics South Africa.
Setting: South Africa, 1897–2019.
Participants: South African.
Results: Pellagra was first officially recorded in South Africa in 1906, but there are earlier indications of the disease. The prevalence of pellagra peaked after it was all but eradicated in the USA and Europe. Pellagra was never as prevalent in South Africa as in Europe, the USA and Egypt, where special hospitals for pellagrins were established. However, studies on urinary excretion of metabolites conducted in 1960s and 1970s suggested a high prevalence of subclinical (sub-pellagra) niacin deficiency, especially in previously disadvantaged Black populations. As in Europe and the USA, pellagra was associated with poverty and an overdependence on maize as staple food. Malnutrition was the main cause of the disease, but alcohol abuse might have been a contributing factor. In South Africa, reports of pellagra had declined by the late 1980s/early 1990s and hardly any cases were reported by the year 2000.
Conclusions: Although pellagra, diagnosed based on dermatological symptoms, appears to be largely eradicated in South Africa, it does not rule out the potential for subclinical niacin deficiency.

Keywords
Pellagra
Malnutrition
Niacin
Nutritional deficiency disease
South Africa

Pellagra is a nutrition deficiency disease, associated with niacin deficiency. The symptoms of pellagra are referred to as the three D's, namely, dermatitis, diarrhoea and dementia, referring to skin, gastrointestinal and neuropsychiatric symptoms, respectively. In the skin, a sunburn-like rash develops symmetrically in areas exposed to sunlight, progressing into thick, scaly, darkly pigmented lesions[1]. Gastro-intestinal symptoms may include inflammation of the mouth and tongue, vomiting, constipation, abdominal pain and diarrhoea[2]. Any of a range of neuropsychiatric symptoms may occur, including apathy, fatigue, depression, confusion, hallucinations, psychosis and memory loss[3]. The symptoms of pellagra may vary, with the classic triad rarely presenting in its entirety[4]. Epidemiological assessment of pellagra is primarily based on dermatological symptoms.

Pellagra was first officially documented in Spain during the first half of the 18th century, but by the second half of the 19th century, it had spread throughout Europe with hundreds of thousands of people contracting the disease[5]. In the USA, pellagra was officially first reported in 1902[5]. About three million people contracted the disease, and over 100 000 died between 1902 and 1940[6,7]. According to the Mortality Statistics of the USA, the prevalence of pellagra peaked in 1928, killing roughly 7000 people in southern America, annually[7]. In Europe, the USA and

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Egypt special hospitals were established to treat those diagnosed with pellagra[5]. Pellagra was largely confined to the poor, who relied on maize as a staple food. With improvements in socio-economic conditions of the working classes and food enrichment, the prevalence of pellagra declined, and by the middle of the 20th century, it had been all but eradicated in large parts of the world[5]. Meanwhile, on the African continent, major outbreaks of pellagra continued to occur. Since 1988, outbreaks of pellagra have been recorded in Angola, Ethiopia, Malawi, Swaziland, Zimbabwe and the Democratic Republic of the Congo, mostly in food-aid-dependent populations such as refugees, internally displaced people, refugee returnee populations and in communities surrounding refugee camps[4]. While the history of pellagra has been well documented in Europe and the USA, much less is known about the prevalence in general populations of sub-Saharan African countries, including South Africa.

The aim of this scoping review was to document the history of pellagra in South Africa, as diagnosed on the basis of dermatological symptoms. Objectives addressed included the prevalence of pellagra over different periods, the main causes of the disease, associations with the consumption of maize and incidences of subclinical (subpellagric) levels of niacin.

Methods

We searched scientific databases, including Academic Search Complete; Africa-Wide Information; AHFS Consumer Medication Information; eBook Collection (EBSCOhost); E-Journals; Family & Society Studies Worldwide; Health Source: Nursing/Academic Edition; MasterFILE Premier; PsycARTICLES; PsycINFO; Social Work Abstracts; TOC Premier, as well CINAHL Complete; MEDLINE Complete; Dentistry & Oral Sciences Source. Initial search words included South Africa, pellagra, niacin deficiency and vit3 deficiency, but varied when specific aspects of the study were investigated.

The structured databases rarely returned findings from the late 19th to early-to-middle 20th century. We thus manually searched through scientific library archives, other archives and record services. We searched websites from reputable organisations such as the South African Medical Research Council; Statistics South Africa (SA); SA Data Archive; the Historical Papers Research Archive, University of the Witwatersrand (Wits); Southern Africa Labour & Development Research Unit, University of Cape Town; the Cory Library Collection, Rhodes University; William Cullen Library, Wits; SA History Online; WHO Regional Office for Africa; National Archives and Record Services of SA.

Further information on the methods employed, including the searches performed and the search strategies, can be found in Appendix 1.

Results

Reports on incidences of pellagra in South Africa

Studies referring to incidences of pellagra in South Africa between 1897 and 2019 are summarised in Table 1.

First reports of pellagra in South Africa

Pellagra first became a problem in 1897, following the outbreak of rinderpest which killed large numbers of cattle in the sub-Saharan region, leading to a marked deterioration in the diets of people[8]. Although cited as the first reference to pellagra, it is doubtful to be the first occurrence. In the 1800's, large areas of southern Africa were marked by severe food shortages and famine, due to war, plant and animal diseases, locusts, as well as severe droughts, which could have resulted in nutritional deficiencies such as pellagra[9,10]. The KwaZulu-Natal region is of special interest, since the first quantitative information on pellagra in South Africa came from there. In 1906, 150 pellagrins were diagnosed from among 3000 Zulu rebel prisoners, captives of the Bambatha uprising, led by Bambatha kaMancinza, leader of the amaZondi clan of the Zulu people. The Bambatha uprising protested against British rule and poll tax in Natal. These prisoners received mainly maize while in captivity, but probably had inadequate diets before capture[11]. Pellagra may also have been prevalent among the general population in KwaZulu-Natal during the late 1800s–early 1900s. A series of pellagra cases were reported in the Tugela valley, KwaZulu-Natal, around 1907, and a Zulu pellagrin, admitted to Addington Hospital, insisted that many individuals with skin lesions similar to his could be found in Zululand[11,12]. There are also suggestions that pellagra was present in the late 1800s–early 1900s in the Transkei. According to a 1940 study, elderly individuals in the Transkei claimed to have been familiar with pellagra symptoms since childhood.

Information from papers in biomedical journals and official documents

Most surveys focused on the Black population[11–64], while fewer studies included two or more races[65–81], and even less centred on the White population only[82–85]. In contrast to Europe and the USA, a significant number of studies involved children, where pellagra was diagnosed based on dermatological symptoms[18,20,24,43,46,52,53,59,60], and studies where niacin status was estimated based on the excretion of urinary metabolites[43,70,71,73,79]. From the mid-1950s onwards, a significant amount of information on the prevalence of pellagra appeared in papers from dermatology services[39,40,45,47,49,50,55–57,64,72,76,80,81,84,85]. Unlike Europe, the USA and Egypt where special hospitals were established for the so-called insane pellagrins[5], in South Africa, a relatively small number of pellagrins were reported in association with neuropsychiatric symptoms[36–38,86–92].

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Table 1 Summary of studies referring to pellagra in South Africa from 1897 to 2019

References	Reports
Bender[8]	1897. South Africa. First mention of pellagra following the outbreak of rinderpest that killed 90 % of cattle in the sub-Saharan region.
Cluver[11]	1906. KwaZulu-Natal. Captives of Dinizulu-Bambatha uprising against British rule and poll tax: 150 pellagrins among 3000 Zulu rebel prisoners.
National Archives[86]	1911. Free State Lunatic Asylum: 5 cases of pellagra over 6 years.
Drummond[12]	1912. KwaZulu-Natal. • Addington Hospital, Durban: one shepherd, fatal • Durban environment: 2 cases in area • Comments to paper: Dr Addison reported several cases in prisoners in Natal, 1906; Dr Knight reported series of cases in 1907 in Nqutu, all coming from Tugela Valley Zululand at time of Zulu rebellion.
Department of Public Health[87]	1912–1913. Pretoria, Pretoria Mental Institution. 60 pellagrins, 15 fatalities.
Mitchel[13]	1913. Transkei: One Black male convict.
Barcroft-Anderson[14]	1913. East London, Cape Province. Coloured girl, died after 180 d.
Swift *et al.*[88]	1914. Bloemfontein asylum, Orange Free State. Six pellagrins in 8 years; all presented with skin, GIT and mental symptoms.
Pijper[82]	1922. Witwatersrand, Transvaal: Four Whites with pellagra.
Barcroft-Anderson[14]	1923. East London Gaol, East London, Eastern Cape. Several Black female pellagrins.
Drummond[83]	1925. KwaZulu-Natal: One case (Roman Catholic sister), fatal.
Cluver[11]	1906–1927. South Africa. Sporadic cases over the period. ±50 cases from Zululand, Natal, Transkei, Witwatersrand.
Cluver[11]	1927 KwaZulu-Natal. Isolated cases of pellagra.
National Arhives[15]	• One Indian male from Amatikulu Leper Institution • Addington Hospital: one Indian female; one 10-year-old Black • Prisons: four males, Congela Prison; one female, Central Prison.
Cluver[11]	1927–1928. Durban, Natal. Pellagra outbreak in Durban Prison Command (Central gaol, Point prison, Congella prison).
National Arhives[15]	64 non-White pellagrins
Cluver[11]	1928. South Africa. After the 1927–1928 prison outbreak, Department of Health requested information on numbers of pellagrins in prisons. • 19 district surgeons attending to prisoners reported 'none' • Krugersdorp and Queenstown gaols: one Black pellagrin each.
Cluver[11]	1928. Addington Hospital, Durban, Natal. • Seven pellagrins • One Zulu pellagrin insisted that there were many more in Zululand.
Cluver[11]	1914–1928. Isolated cases documented by EH Cluver. • East London gaol: 1914 Coloured convict; 1915 Coloured convict • Durban, Natal: 1920 White citizen; 1922 White citizen • Witwatersrand 1927: one White, one Black pellagrin • Natal 1927: one Black at Amatikula; three Blacks at Addington Hospital.
Editorial[65]	1930. Editorial without relevant references: 'Pellagra endemic but misdiagnosed'.
MacVicar[16]	1935. Ciskei • Isolated mild cases of pellagra. • Editor's comment to MacVicar paper: 'Pellagra common in Ciskei, but not diagnosed'.
Heiman[17]	1936–1939. Non-European Hospital, Johannesburg.
Kark *et al.*[18]	• Increase in number of cases over period from 1937 to 1939. • 1937: 23 cases; 1938: 40 cases; 1939: 66 cases of pellagra.
Suzman[19]	1935–1941. Johannesburg Hospital. • Increased cases from 1935 to 1941. • 1935: 7; 1936: 4; 1937: 25; 1938: 52; 1939: 68; 1940: 92; 1941: 101 cases.
Kark *et al.*[18]	1938–1939. Survey of 7000 Black schoolchildren (˜800 in each of three urban and six rural areas).
Kark *et al.*[20]	Total number of pellagrins: 131; prevalence 1·84 %. • Transvaal: Pretoria 1 pellagrin (0·12 %); Letaba 1 pellagrin (0·12 %); Bochem 117 pellagrins (14·8 %) • Orange Free State: Bloemfontein 3 pellagrins (0·36 %); Witzieshoek 1 pellagrin (0·14 %) • Natal: Pietermaritzburg 0 pellagrins (0 %); Nqutu 1 pellagrin (0·13 %) • Transkei: Qumbu 2 pellagrins (0·24 %); Kentani 5 pellagrins (0·62 %).
Kark *et al.*[20]	1939. Community Centre, Pholela, Transkei. Communication to author. • Pellagra common in Idutywa district, Transkei (Soga, 1938) • Several pellagrins at. Paul Roux, Orange Free state (Kristal, 1939) • Pellagra common in Durban non-European hospitals (Dormer, Murray, 1939) • In Transkei pellagra misdiagnosed as venereal disease (Daneel, 1939).
Fox[21]	1939. South Africa: Reports of pellagra increased due to better diagnosis.
Mears[22]	1942. Tsolo, Transkei. Verbal reports by rural Blacks. • Keleba (pellagra) endemic in Tsolo district, said by locals & medical staff • Older locals familiar with the symptoms since childhood

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Table 1 *Continued*

References	Reports
Mears[23]	1942. Tsolo, Transkei. Pondomisi and Fingo tribes. • 59 cases of Keleba, identified as pellagra • 90 % of 59 from Pondomisi tribe (higher alcohol intake)
Gillman *et al.*[24]	1942–1945. Non-European Hospital Johannesburg. 180 Black infant pellagrins under investigation and treatment for hepatic damage.
Kark *et al.*[20]	1943. Urban area Johannesburg and rural areas of Pholela and Impendle, Natal.
Kark[25]	• 96 cases: 34 infants and 62 adults • More common than in previous 10 years.
Luckhoff[26]	1943. Orange Free State. 4600 Blacks from general population surveyed. Pellagra in 30 (0·65 %).
Gillman *et al.*[28]	1942–1945. Personal communication to Gillman and Gillman. • 1942–1944. Rietfontein (Sizwe) Hospital: 1942: 58 cases; 1943: 76 cases; 1944: 97 cases (Sacks) • 1944 Durban hospital and area, endemic (Dormer) • 1945 Pretoria Hospital, endemic (Jansens)
Gillman *et al.*[28]	1942–1944. Johannesburg hospital and environment. • Increase in number of cases from 1942 to 1944 • 1942: 115 cases; 1943: 148 cases; 1944: 238 cases
Gillman *et al.*[28]	1944. Johannesburg area: 120 pellagrins, 1 % mortality.
Gillman *et al.*[28]	1906–1945. Union of South Africa and *Protectorates. Author estimation, based on published reports, personal communication and own research. • 2000 cases of pellagra over period 1906–1945 *(Basutoland (Lesotho), Bechuanaland (Botswana), Swaziland (Eswatini))
Gillman *et al.*[28]	1941–1945. Johannesburg area & Transkei. Calculated from figures of Gillman and Gillman for Johannesburg Hospital area and Tsolo, Transkei. • Johannesburg area 1935 to 1941: 349 cases • Johannesburg area 1942 to 1944: 785 cases • Transkei (Tsolo district): 418 cases identified for 1944–1945
Gillman *et al.*[29]	1945. Johannesburg. UV fluorescence microscopy of frozen sections of liver fragments from twenty African pellagrins.
Gillman *et al.*[30]	1942–1947: Review by Gillman and Gillman (include previously reported). • 1942–1945: >2000 patients treated for pellagra, Johannesburg Hospital • 1943–1947: 4000 cases of pellagra seen in South Africa • Seasonal occurrence: Highest prevalence mid-summer (November/December) • Association with maize as staple food
Minde[89]	1946. Fort Beaufort Asylum, Eastern Cape. • Hypovitaminosis, e.g. pellagra • Malnutrition ascribed to ravages of WW II and local droughts
Walker[31] Kropman[32]	1946. Niacin levels in breast milk: 12 Black mothers 108 μg/100 ml; American mothers' average 268 μg/100 ml.
National Archives[33]	1949–1950. Mandhleni, Tembu Ward, Msinga District, KwaZulu-Natal. • Outbreak of pellagra involving 55 families • Several fatalities.
Jackson[34]	January 1952. Tabankulu, East Pondoland, Transkei. • 13 Pellagrins among 90 Black patients seen in surgery, 14·4 % • 1 Pellagrin among 520 male labourers, 0·2 % • 5 Pellagrins among 19 in township during disease outbreak, 26 %
Kark *et al.*[35]	1952. Pholela Health Centre, Bulwer, Natal. Progress report: Dramatic decline in pellagra after introduction of health care services & vegetable gardens.
Lamont *et al.*[36]	1952. Weskoppies Mental Hospital, Pretoria. 258 Black males admitted, 22 (8·5 %) diagnosed with pellagra psychosis.
Lamont *et al.*[37]	1951–1953. Weskoppies Mental Hospital. Pretoria. 295 observation cases facing criminal charges: 4 (1·35 %) diagnosed with pellagra.
Moffson[38]	December 1952–February 1954. Weskoppies Mental Hospital, Pretoria. 400 Black men admitted: 5 (1·25 %) psychotic due to chronic malnutrition/pellagra.
Barnes[66]	1955. Johannesburg industrial areas. 95 patients investigated for potential porphyria: 26 (27 %) diagnosed with pellagra.
Findlay[39]	1956. Non-European Dermatology Outpatients, Pretoria Hospital. 600 consecutive patients. • Nutritional deficiency diseases (mainly pellagra): 30 patients (5 %) • Chronic alcoholism sometimes a predisposing factor.
Findlay *et al.*[84]	1955–1959. Transvaal & Orange Free State. 13 500 Whites. • 4500 Dermatology Outpatients, Pretoria Hospital • 5000 Private Dermatology Practice Pretoria • 4000 Private Dermatology Practice Bloemfontein • Overall pellagra prevalence = 0·05 % (7/13 500)
Schultz *et al.*[40]	1956–1961. Transvaal and Orange Free State. 4000 Black patients. Pellagra prevalence: • 1956: Dermatology Outpatients, Pretoria (30/600) 5 % • 1959–1961: Dermatology Outpatients, Pretoria (126/2000) 6·3 % • 1958–1961: Dermatol. Outpatients, Bloemfontein (63/1000) 6·3 % • 1958–1961: Inpatients Pretoria (10/400) 2·5 %

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Table 1 *Continued*

References	Reports
Potgieter *et al.*[67] Potgieter *et al.*[68]	1960. Questionnaires to all registered doctors. 253 questionnaires returned, each could contain responses from 10 doctors. Two 4-week periods (May/June and November/December) collections. Prevalence of pellagra: • 3132 pellagrins among total of 195 175 patients (1·6 %) • Witwatersrand/Pretoria: Black (814/58 2091) 1·4 %; Coloured (0/1557) 0 % • Rural Transvaal: Black (758/22 300) 3·4 %; Coloured (0/73) 0 % • Cape town/Peninsula: Black (14/1622) 0·9 %; Coloured (6392) 0 % • Transkei: Black (567/26 996) 2·1 %; Coloured (0/492) 0 % • Rural Cape Prov.: Black (18/3508) 0·5 %; Coloured (0/8358) 0 % • Natal: Back (818/51 134) 1·6 %; Coloured (0/1784) 0 % • Orange Free State: Black (160/12 333) 1·3 %; Coloured (0/420) 0 %
Potgieter *et al.*[67] Reid[69]	1960. 1971 Cory Library paper. Estimation based on National Nutrition Research Institute Survey: Pellagra in Blacks and Coloureds ˜26 000/year.
Neser[41]	1963. Congress presentation. Estimations based on personal communication with deputising medical doctor, summer 1963. • Pellagra in 50 % of patients in Hammanskraal (Bantu reserve) • Similar situation in Sekhukhuniland (Bantu reserve) • Incidence higher in summer than in winter.
Quass[42]	1965. Opening address, South Africa Nutrition Society. No reference. • Pellagra ≥50 % of patients at medical clinics in Bantu reserve areas • Pellagra in many patients of hospitals at mission hospitals. • Pellagra in 50–75 % of admissions to mental hospital in Pretoria
Du Plessis *et al.*[70] Du Plessis *et al.*[71]	1962–1965. Pretoria area. Urban Schoolchildren. Nicotinic acid status (urine ratio of 2-pyridone:N^1-Me). Latent (subclinical) nicotinic acid deficiency varied with race and age: • 1962: 464 White children tested. 7–11 years deficiency in 14·1 % • 1963: 585 Black children tested. 7–11 years deficiency in 53·1 %; 12–15 years deficiency in 35·6 % • 1964: 442 Coloured children tested. 7–11 years deficiency in 32 %; 12–15 years deficiency in 29 %; • 1964: 366 Indian children tested. 7–11 years deficiency in 24·6 %; 12–15 years deficiency in 37·7 % 1965: 248 White children tested. 12–15 years deficiency in 5·6 %
Marshall *et al.*[72]	1962–1963. Cape Province. 4000 dermatology patients. Pellagra prevalence: • 1000 Whites, Cape Town private practice, 0 % • 1500 Whites, Carl Bremer Hospital, Cape, 0 % • 1500 Coloureds, Carl Bremer Hospital, Cape, 1·3 %.
Prinsloo *et al.*[43]	1962–1964. Pretoria General Hospital. Black Children • 56 pellagrins (4–12 years) • Diagnosis confirmed by urine metabolites.
Jones[90]	1963. Sterkfontein Psychiatric Hospital: ≥30 pellagrins.
Ross[44]	1964. Northern Province, Venda Homeland. 2000 Vendas, all ages. Seen at Donald Fraser Mission Hospital; outpatients clinic run by hospital at Sibasa; Tshilidzini Mission Hospital; villages of Thenga, Rambuda and Makula; and at schools adjacent to the villages. • Pellagra (magidiphoo): (28/2000) 1·4 % • Locals attribute symptoms of pellagra to drinking of *muvanya* (sugared beer) and *thothotho* (a home distilled alcoholic drink) • None in children 2–16 years old (supplementary feeding at school).
De Lange *et al.*[73]	1964. Pretoria. Schoolchildren. Niacin status assessed by urinary excretion of metabolites. • Deficiency/near deficiency of nicotinic acid in majority Black primary schoolchildren; none in White primary schoolchildren.
Findlay[85]	1955–1965. Transvaal, mainly Pretoria. 165 000 White patients from private practice and outpatients Pretoria Hospital. • Incidence below 1 %.
Park[45]	1965–1968. Pretoria Hospital. 3798 Black dermatology outpatients. • Overall pellagra prevalence 3·0 % • Proportion according to age: 0–4 years, (15/500) 3 %; 5–9 years, (13/413) 3 %; 10–14 years, (8/384) 2 %; 15–19 years, (10/510) 2 %; 20–24 years, (6/599) 1 %; 25–29 years, (9/447) 2 %; 30–34 years, (17/276) 6 %; 35–39 years, (7/230) 3 %; 40–44 years, (10/198) 5 %; 45–49 years, (7/135) 5 %; 50–54 years, (3/83) 4 %; 55–9 years, (0/45) 0 %; ≥ 60 years, (4/85) 5 %
Pretorius[46]	1966. Pretoria. HF Verwoerd Hospital. 5092 Black paediatric admissions (<12 years of age): 22 diagnosed with pellagra, 0·4 %.
Van Heerden *et al.*[160]	1966. Johannesburg. Coronation Hospital. • 12 coloured pellagrins tested for potential impaired fat absorption • Five were chronic alcoholics
Findlay *et al.*[47]	1968. Transvaal. Pellagra as % of common skin diseases in 220 000 dermatology outpatients as compiled by authors from previous papers. Pellagra incidence in Black patients (*n* = number of patients seen): • <4 years (*n* 500): 3 %; 5–9 years (*n* 413): 3 %; 10–14 years (*n* 384): 2 %; 15–19 years (*n* 510): 2 %; 20–24 years (*n* 599): 1 %; 25–29 years (*n* 477): 2 %; 30–34 years (*n* 276): 6 %; 35–39 years (*n* 230): 3 %; 40–44 years (*n* 198): 5 %; 45–54 years (*n* 218): 5 % ; ≥55 years (*n* 130): 4 % • No White or Indian patients with an incidence ≥1 %

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Table 1 *Continued*

References	Reports
Nel *et al.*[48]	1968. Venda Homeland. 500 Venda males, fair nutritional state. Nicotinamide deficiency according to urine metabolites. • 253 rural Venda males: subclinical deficiency in 60 % • 247 urban Venda males: subclinical deficiency in 47 %
Dogliotti[49]	December 1968–November 1969. Baragwanath Hospital, Johannesburg. • 44 pellagrins among 2000 Black dermatology outpatients: (2·2 %) • 11 pellagrins out of 400 inpatients (2·75 %).
Dogliotti[50]	1969–1972. Johannesburg, Baragwanath Hospital, Dermatology services. 9474 first consultation Black patients over 3 years period. • 188 pellagrins among 9474 patients (1·98 %) • Incidence in adults related to alcohol consumption. • Age-dependent frequency. • % of pellagra patients per age group: 0–10 years (2 pellagrins): 1·1 %; 11–20 years (4 pellagrins): 2·1 %; 21–30 years (53 pellagrins): 28·1 %; 31–40 years (73 pellagrins): 38·8 %; 41–50 years (41 pellagrins): 21·8 %; 51–60 years (12 pellagrins): 6·4 %; 61–70 years (2 pellagrins): 1·1 %; 70 years+ (1 pellagrin): 0·5 %.
Cole[91]	1970–1973. Sterkfontein Mental Hospital. 200 autopsies, 11 pellagrins.
Louw *et al.*[51]	1970–1971. Rural (August 1970), urban (March 1971) adult Pedi men. Niacin status based on urine 2-pyridone:N^1-Me ratio. Low niacin status in: • 77 % of 204 rural Pedi men from Chieftaincy of Paramount Chieftainess Mankopodi Thulare Sekhukhune, Mohlaletsi, Lydenburg • 50 % of 239 urban Pedi men, Katlehong Township, Germiston.
Du Plessis *et al.*[52]	1971. Pietersburg (Polokwane). Black Higher Primary School, children. • Boyne: 9 pellagrins among 70 children (13 %) • Seshego village: no pellagrins among 70 children
Hankes *et al.*[74]	1971. 250 miles radius from Pretoria: 16 pellagrins all with Casal's collars.
Prinsloo *et al.*[53]	1971. Pretoria. HF Verwoerd Hospital: 12 Black children with pellagra.
Van der Merwe[161]	1971. Venda. Study on nutritional status of 257 rural and 248 urban Venda males. • 7 % of rural and 2 % of urban subjects had pellagra • Overt symptoms only in subjects ≥40 years of age.
Prinsloo *et al.*[162]	1971. Pretoria, HF Verwoerd Hospital. • 15 children with pellagra (9 boys, 6 girls) examined for glucose tolerance and insulin sensitivity.
Rose *et al.*[54]	1972. Transkei & Ciskei. 8684 (3496 males; 5188 females) first time Black patients at 12 hospitals over two consecutive weeks January/February. • 24 male pellagrins (0·7 %) • 103 female pellagrins (2 %)
Walker[75]	1972 South Africa. Author's estimate of pellagra: Blacks +++; Whites –
Schultz[55]	1974–1980. Ga-Rankuwa Hospital, Pretoria. 5000 Black dermatology patients seen in 6 years.
Schultz *et al.*[56]	• Pellagra prevalence as % of total skin diseases: 1·7 %
Park[45]	• Progressive decline 1961: 6·3 %; 1968: 3 %; 1982: 1·7 %.
Krengel[92]	1975. Boksburg/Benoni Hospital, Transvaal. 42 pellagrins investigated for neuropsychiatric symptoms (38, alcohol abuse; 26, low protein intake).
Flöter[76]	1975. Tygerberg Hospital, Western Cape. 3797 dermatology outpatients. • Adult Whites: 0 % pellagra • Adult non-Whites: 0·1 % pellagra.
Metz *et al.*[77]	1976/1978. South Africa. • Authors state that, according to communication with Department of Health, ≥100 000 patients were annually treated for pellagra, as inpatients or as outpatients • Supporting documentation could not be found
Dogliotti *et al.*[57]	1977. Baragwanath Hospital, Johannesburg. Sebum composition measured in 51 pellagrins.
Segal *et al.*[58]	1978–1986. Baragwanath Hospital, Johannesburg. GIT studies • 45 pellagra patients studied for rectal manifestation of pellagra • GIT inflammation in 42
Saldru Working Paper[59] Du Plessis *et al.*[60]	1978. Ciskei, 713 randomly selected children (6 months to 8 years) from 10 rural areas. Prevalence of pellagra: 6 months to 2 years: 1·1 %; 3–4 years: 1·3 %; 7–8 years: 6 %.
Seymour[163]	1979. East Griqualand. Private practice. • Unspecified number of pellagrins attending practice • Mental problems without skin lesions appeared more commonly in winter than in summer.
Paine *et al.*[78]	1940–1980. 14 pellagrin skeletons from Raymond Dart Skeletal Collection. Macro- and microstructural indicators suggested a niacin-deficiency-associated demineralisation.
Ndaba[61]	1975–1984. KwaZulu-Natal (Second Carnegie inquiry into poverty and development in Southern Africa). Alcohol abuse described as major contributor to pellagra. Number of pellagrins admitted to hospitals: • Ceza Mission Hospital: 1980: 4; 1981: 6; 1982: 9 • Charles Johnson Hospital Nqutu: 1975: 74; 1976: 100; 1977: 59; 1978: 66; 1979: 32; 1980: 53; 1981: 41; 1982: 46 • Eshowe Hospital: 1978: 69; 1979: 72; 1989: 87; 1981: 62; 1982: 9.

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Table 1 *Continued*

References	Reports
	• Kwa Magwaza Hospital: 1978: 31; 1989: 27; 1981: 36; 1982: 22 • Maphumulo Hospital: 1975: 8; 1976: 16; 1977: 15; 1978: 9; 1979: 11; 1980: 17; 1981: 13; 1982: 16 • Mbongolwane Hospital, Ntumeni: 1982: 12 • Ngwelezane Hospital & Ngwelezane Health Ward: ˜ 20 cases/year • Nkandla Hospital: 1978: 9; 1979: 8; 1980: 25; 1981: 18; 1982: 23 • Nkonjeni Hospital: 1979: 15; 1980: 13; 1981:10; 1982: 26 • Stanger Hospital: 1978: 104; 1980: 98; 1981: 123; 1982: 93
Soldenhoff *et al.*[79]	1988. Transvaal. Niacin status (urinary 2-pyridone) in 75 schoolchildren (25 in each group). • Subclinical deficiency: White middle class, 4 %; Indian, low socio-economic, 12 %; Rural Black village, 28 %.
McCabe[62]	1989. Polyclinic, Department of Family Health, Kalafong Hospital. Five alcoholics diagnosed with pellagra.
Segal *et al.*[63]	1990. Baragwanath Hospital, Johannesburg. Nine pellagrins studied for pathology of the oesophagus.
Walker[127]	1995. South Africa: Review. Walker claims sharp decline in prevalence.
Hartshorne[80]	1999. Johannesburg. Retrospective study. 7029 dermatology outpatients at five academic hospitals (Johannesburg, Chris Hani Baragwanath, Hillbrow, Helen Joseph and Coronation hospital). Prevalence of pellagra: • Black patients 0·2 % • White, Coloured and Indian patients 0 %.
Dlova *et al.*[64]	2003–2010. Durban, KwaZulu-Natal. 6664 Black patients attending single private practice over 7 years. • Pellagra prevalence 0 %.
Dlova *et al.*[81]	1 January–31 March 2013. KwaZulu-Natal. 3818 patients with skin diseases from public referral hospitals (69 % African, 24·7 % Indian, 6·3 % White or Coloured). • Pellagra prevalence 0 %.
Statistics South Africa[106]	1997–2016: Pellagra mortality per annum: 1997: 86; 1998: 79; 1999: 65; 2000: 74; 2001: 63; 2002:60; 2003: 61; 2004: 37; 2005: 32; 2006; 29; 2007: 14; 2008: 17; 2009: 20; 2010; 12; 2011: 11; 2012: 5; 2013: 7; 2014: 2; 2015: 5; 2016: 5.

Estimations from burden of disease based on hospital admissions and causes of death

Papers in scientific journals on burden of disease as reflected by hospital admissions did not return any relevant information; pellagra was not named among the leading ten or twenty causes of admission[93–102]. Most of these papers covered hospitals serving disadvantaged communities, where malnutrition, and therefore pellagra, would have been the most prevalent. Our own findings are corroborated by that of a systematic review on causes of admission to hospitals from 1950 to 2010[103].

Records on the causes of death should shed some light on the burden of disease in a country. In a well-referenced book by Van Rensburg and Mans on disease profiles during the 1970s[104], pellagra does not appear among the top causes of death for any population group. Neither does pellagra feature in a 2016 publication by the Medical Research Council on cause-specific death rates for the period 1997–2012[105]. According to Statistics SA, 684 people died from pellagra over the 20-year period from 1997 to 2016. A progressive decline in pellagra-associated deaths is recorded with eighty-six in 1997 down to five in 2016[106].

Discussion

As for Europe, Asia, Egypt and the USA[5], the prevalence of pellagra in South Africa is intertwined with the socio-political history of the country. In South Africa, pellagra was mainly recorded in disadvantaged populations where maize represented the staple food without augmentation with adequate fresh vegetables and protein[11,18,28,30,32,107].

Prevalence over different periods

1700s/1800s: Despite several natural and man-made disasters over the 18th and 19th centuries[107], there is only one record of pellagra, namely, the outbreak of pellagra following the rinderpest epidemic of 1897[8]. The dearth in reports could be due to the fact that most health care was, with exception of the Cape settlement, provided by traditional healers and, later on, missionaries. By the end of the 19th century, South Africa had a mere 650–700 Western trained medical doctors of whom more than 60 % lived in the Cape area[108,109].

1900–1930: During the first three decades of the 20th century, several events occurred that gave rise to food shortages and malnutrition[110,111], but are not reflected in reports on incidences of pellagra. This period also saw the creation of Black reserves through a series of discriminatory acts, e.g. the controversial Land Act of 1913 that made it illegal for Black Africans to purchase land except in demarcated reserves or to work as sharecroppers[110,112].

Over the three decades, three outbreaks of pellagra were recorded, but never nearly of the magnitude seen in Europe or the USA. The first outbreak (1906) occurred among prisoners of war when 150 pellagrins were identified by Dr LG Haydon among 3000 Zulu prisoners of

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war[11]. The second outbreak (1912–1913) occurred in the Pretoria Mental Institution where sixty inmates were diagnosed with pellagra[11,87], and the third outbreak (1927–1928) involved sixty-four Black prisoners from three prisons in the Durban Prison Command diagnosed by Drs Rhodes and English[11,15]. An estimated fifty more sporadic cases were officially diagnosed, mainly from Zululand, Natal, the Transkei and a few from the Johannesburg area[11]. However, verbal reports, both from medical personnel and locals, suggest that pellagra may have been more prevalent[11,22,65]. There are also indications that subclinical deficiency of niacin may have been common in certain areas, especially in Black reserves[11,113]. According to census data, the population of South Africa numbered 16 928 580 in 1921[114].

1931–1947: Over the following 17 years, the frequency of reports on the prevalence of pellagra, as well as the number of pellagrins for specific areas, increased[17–19,21,28,29]. In general, malnutrition and malnutrition-related diseases were by now common among the poor[115–118]. The increase in the number of reported pellagra cases may partly have resulted from the founding of community health centres[108,117,119]; an increase in the doctor:patient ratio from 1:3600 in 1930 to 1:2427 in 1946[104] and an increase in the number of community health surveys between 1930 and 1947[20,115,117]. Pellagra was recorded in large community studies primarily focusing on Black children. The recorded prevalence in those studies varied widely between areas. For instance, in a 1938/1939 study by Kark and Le Riche[18,20] involving about 7000 Black schoolchildren in urban and rural areas of the Transvaal, Orange Free State, Natal and the Transkei, a total of 131 (1·87 % of 7000) cases of pellagra were reported, with figures varying between 0 % and 14·83 % for different regions. No such studies exist for adults.

From records of hospitals and clinics, and from verbal reports by locals who referred to pellagra as *kelaba*, it appears that pellagra may have been endemic in areas of the Transkei such as Idutywa and in Tsolo where 418 cases were diagnosed in the 1940s[22,23,28]. Pellagra was not uncommon in the Ciskei[16], but due to a scarcity of medical services, records are not available. Better records are available for Johannesburg which had far better medical services and a medical school. While only isolated cases were reported in the Johannesburg area during the 1900–1930 period, at least 500 patients were diagnosed with pellagra between 1935 and 1941[17–20], and according to our calculations, about 1000 cases over the 1942–1945 period (Table 1). However, Gillman and Gillman[30] who were by then studying pellagra in South Africa and had access to unpublished data estimated that more than 2000 patients were treated for pellagra at Johannesburg Hospital over the 1942–1945 period. Based on their own observations and that of others, Gillman and Gillman[30] further estimated 4000 cases of pellagra in South Africa between 1943 and 1947, which can be extrapolated to approximately 1000 per annum, mostly in the Black population.

1948–1994: When in 1948, the National Party came into power; it institutionalised and expanded on the apartheid policies of preceding decades. The Promotion of Bantu Self-Government Act of 1959 proclaimed the existence of eight African ethnic groups with the aim of developing self-governing Black Homelands (Bantustans), independent of White intervention[110,112]. This culminated in two homelands for the Xhosa, namely, Ciskei and Transkei; Bophuthatswana for the Tswana people; KwaZulu for Zulu people; Lebowa for the Pedi and Northern Ndebele; Venda for Vendas; Gazankulu for Shangaan and Tsonga people and Qwa for Basothos[110,112,120]. The Black homelands were characterised by poor economic conditions before and after establishment, lack of infrastructure, limited employment opportunities which forced many to become migrant labourers, large-scale corruption and the growth of a Black middleclass bureaucratic elite. These factors contributed to poverty and malnutrition in the general homeland populations[110,120,121].

Confusion exists about the prevalence of pellagra during the 'era of high apartheid' (1948–1976). Uncorroborated reports[4,41,42,77,122–124] suggest that pellagra reached epidemic proportions throughout South Africa during the 1970s. We found, for this period, reliable sources for at least 4500 cases of pellagra out of 276 000 observations, an estimated prevalence of 1·63 % (Table 1). In 1960, in an attempt to estimate the national prevalence of pellagra, a questionnaire was sent by the National Research Institute to all registered medical practitioners, requesting information on patients seen over two 30-d periods, namely, a summer period and a winter period[67,68]. Two hundred and fifty-three correctly completed questionnaires (each questionnaire containing records of up to ten doctors) were returned. These appear to be mainly from doctors in areas where malnutrition and diseases of malnutrition were common, such as the Black reserve areas of Zululand, the Transkei and Northern Transvaal. Of the 195 175 patients documented in the survey, 3132 were diagnosed with pellagra, an estimated prevalence of 1·6 %.

We suspect that many cases of pellagra went unpublished, such as the 1949–1950 outbreak of pellagra at Mandhleni, Msinga District, in the then Zululand[33]. Msinga is an isolated, poverty-stricken area, located in deep gorges of the Tugela and Buffalo Rivers in an area that later became part of the KwaZulu Homeland. We only found evidence on the Msinga outbreak in the National Archives, in letters to and from the medical superintendent at Tugela Ferry. During the Msinga outbreak, fifty-five families are said to have contracted pellagra with an unspecified number of fatalities[33].

From 1948 to 1994, the population more than trebled from 11 957 000 in 1948 to 38 631 000 by mid-1994[125]. Over this period, an estimated 7000 cases of pellagra were

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officially documented, with a prevalence of 1·75 % among the more than 400 000 individuals surveyed (Table 1). Many of the surveys focused on areas and groups with known malnutrition, and figures can thus not be extrapolated to represent national prevalence. More unreported incidences probably occurred, especially in areas with inadequate medical services such as the Black homelands[104,116]. To illustrate, by 1962, only 2·8 % of fulltime medical doctors in South Africa worked in the homelands, which grew to 4·8 % by 1974. The doctor:population ratio in the homelands was estimated at 1:15 000, in contrast to 1:1969 in rest of South Africa[104].

Decline in the prevalence of pellagra

Indications from clinics and hospital records are that the prevalence of pellagra in urban areas started to decline towards the 1970s. However, attendance records at dermatological services suggest that the number of patients suffering from pellagra in metropolitan areas already began to decline in the late 1960s. In large hospitals in the Pretoria area, the proportion of dermatological patients suffering from pellagra declined from 6·3 % in 1962 to 3 % in 1968, to below 1·7 % over the 1974–1980 period[45,55,56]. The proportion of Black dermatological patients diagnosed with pellagra at Chris Hani Baragwanath Hospital, the largest hospital in Africa, declined from 2·2 % between 1968 and 1969 to 1·98 % between 1969 and 1972[49,50]. The early decline observed in metropolitan areas may merely reflect differences in nutritional status between rural and urban populations[126]. Elsewhere, pellagra continued to occur, especially in the Black homelands. In 1975, a 2-week survey of twelve hospitals in the Ciskei and Transkei found 127 pellagrins out of 8684 patients (1·46 %)[54]. A retrospective study of ten hospitals in rural KwaZulu-Natal found that 514 pellagrins were admitted over a 9-year period from 1975 to 1984[61]. It is important to note that the figures only reflect those who attended hospitals.

All indications are that, by the late 1980s, early 1990s, the prevalence of pellagra was declining throughout South Africa. In a 1995 review of nutrition-related diseases, Walker[127], perhaps a little too optimistically, wrote 'In the past this deficiency disease was common in rural areas. Its current prevalence is much lower. In big towns it is no longer seen'. By the end of the 20th century, very few papers even mentioned pellagra. In 1999, a retrospective study of 7029 dermatology patients at five academic hospitals in the Johannesburg area showed a pellagra incidence of 0·2 % for Black patients and 0 % for the White, Coloured and Indian populations[80]. In KwaZulu-Natal, no cases were diagnosed among 6664 Black private practice patients over 7 years between 2003 and 2010[64], or among 3818 dermatological patients seen over 3 months at public referral hospitals in 2013[81]. Mortality data from Statistics SA showed decreased mortality due to pellagra, from eighty-six cases in 1997, to twelve cases in 2010, remaining below ten per year from 2012 to 2016[106].

Several factors probably contributed to a decline in the prevalence of pellagra as diagnosed by dermatological symptoms. Improvement in the socio-economic circumstances and social grants, as well as the food fortification initiatives and social and food security programmes, undoubtedly had a positive impact. For more information on the many food security initiatives, the reader is referred to a document from 'Feed the Future Innovation Lab for Food Security Policy'[115]. A brief account on the South African food fortification initiatives, particularly the fortification of maize meal, can be found in the section dealing with pellagra and the consumption of maize in South Africa.

Subclinical levels of niacin

Subclinical (sub-pellagra) levels of niacin deficiency in South Africa were inferred as early as late 1920s to early 1930s. Deficiencies were implied by the rapidity with which some prisoners in Natal gaols developed pellagra when subjected to inadequate prison diets[11], and by the appearance of pellagra symptoms when newly arrived migrant labourers from Black reserve areas started to work on the mines[113]. The first problem was remedied by a change in prison diets[11] and the second, by a period of rest on nutritionally adequate diets before engaging in the labour of mining[113].

During the second half of the 20th century, the existence of subclinical niacin deficiency was confirmed by urine analysis. Over the period 1962–1965, the nicotinic acid status based on urinary excretion of N^1-methyl nicotinamide (N^1-Me) and N^1-methyl-2-pyridone-5-carboxylamide (2-pyridone) was determined in 2105 urban schoolchildren between the ages of 7 and 15 years in the Pretoria area[70,71]. A 2-pyridone:N^1-Me ratio of <1was considered as indicative of latent nicotinic acid deficiency[70,71]. The study included the four main racial groups and found, depending on the area, latent niacin deficiency in 5·6–14·1 % White, 24·6–28·7 % Indian, 28·7–32 % Coloured and 35·6–53·1 % Black children[70,71]. Other studies on primary schoolchildren showed niacin and riboflavin deficiencies[71,73] for Black, but not White children. We found only two studies investigating niacin levels in adults. The first, a 1969 study of 500 Venda men reported a fair nutritional status, but suboptimal nicotinamide levels in 60 % (151/253) rural and 47 % (116/247) urban Venda men[48]. The second study conducted in August 1970 and March 1971 reported low niacin status in 77 % (157/204) rural adult Pedi men from Mohlaletsi, Ehlanzeni District, Mpumalanga Province, and in 50 % (120/239) urban adult Pedi men from Katlehong Township, Ekurhuleni, Gauteng Province[51]. Studies conducted in the 1970s showed that fortification of maize meal with niacin and riboflavin could alleviate subclinical niacin deficiency[128].

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It is important to note that the above subnormal levels of niacin reported were generally found in populations with no visible dermatological symptoms of pellagra. Today, the diagnosis of pellagra and epidemiological estimates of niacin deficiency are still largely based on the dermatological symptoms of the disease. In view of the fact that niacin is the precursor of the all-important coenzyme NAD and that niacin and NAD deficiencies can influence virtually all physiological processes, from cerebral functions to genomic stability, this is rather disconcerting.

Pellagra and consumption of maize in South Africa

As a nutrition deficiency disease, pellagra is primarily associated with a deficiency in niacin. In Europe, the USA and Egypt, outbreaks of pellagra were often observed when maize became the staple food in near monophagic diets of the poor[5]. Most of the niacin present in maize is found in the aleurone, germ and endosperm, bound up in a hemicellulose complex that is nutritionally unavailable to humans. These niacin-containing fractions are lost during industrialised milling processes[5,129]. Maize, furthermore, contains a limited amount of bio-available tryptophan, the precursor for *in vivo* synthesis of niacin.

As elsewhere, an association has been observed in South Africa between pellagra and nutritionally inadequate maize-based diets[11,20,21,28,30,43,72,118]. However, there are several noteworthy differences. Maize apparently became the primary staple food much later in South Africa than in Europe, and marginally later than in the USA[5,11,107]. In KwaZulu-Natal, millet, as part of a multi-crop food source, was still the primary grain by the middle of the 19th century[107]. At the turn of the century, maize had become the dominant crop in KwaZulu-Natal[11], and the major grain in the Transkei by 1936[107]. In South Africa, the practice of crude stone grinding, instead of industrialised milling, has been suggested to contribute to the relatively low incidence of pellagra in the 19th and early 20th centuries[11]. In addition, consumption of green maize, boiled or roasted, in which the endosperm is still soft and the nutrition bio-availability higher, forms an important part of maize consumption in Africa. Furthermore, traditional African food preparation processes such as fermentation and roasting increase the bioavailability of niacin[130,131]. Fermented maize, for instance, has almost double the riboflavin and niacin content of unfermented maize[132]. Many fermented foods are traditionally consumed in Africa[133], including non-alcoholic beverages such as Mahewu, and alcoholic beverages such as Umqombothi[133–135]. Drinks, made from fermented maize, are consumed by both adults and schoolchildren and in certain cultures are used as a weaning food for infants[133–135].

What cannot be denied is that maize is, and has long been, a staple food in the country[11,20,21,28,30,43,72,118] and that inadequacies of a diet over-dependent on maize can contribute to nutritional deficiencies such as pellagra[5]. In South Africa, provisional maize meal enrichment programmes started as early as the 1960s[136] and in the 1970s studies were conducted which showed that fortification of maize meal with niacin and riboflavin could indeed alleviate subclinical niacin deficiency[128]. Attempts to remedy the inadequacies of a diet over-dependent on maize by voluntary fortification by industries have met with some success, but maize meal samples sourced during the last quarter of 1986 from stores in the erstwhile Transvaal, Orange free State, Natal, Eastern Cape Province and Transkei showed concentrations of nicotinic acid and riboflavin to be well below the recommended levels[137,138]. In April 2003, regulations regarding mandatory fortification of all maize meal and wheat flour were printed in the Government Gazette, published under Act No 54 of 1972[139]. Fortification of maize meal and wheat flour with vitamin A, thiamine (vitamin B_1), riboflavin (vitamin B_2), niacin (vitamin B_3), pyridoxine (vitamin B_6), folic acid (vitamin B_9), Fe and Zn became mandatory on the 7 October 2003, with cyanocobalamin (vitamin B_{12}) later added to the list. Despite indications from post-implementation studies that suggest suboptimal compliance with statuary fortification requirements at mills[138,140], indications are that fortification of maize meal markedly improved the intake of micronutrients such as niacin[138,141].

Causes of pellagra in the South African population

Although pellagra is generally associated with diets inadequate in niacin, niacin is also synthesised from the essential amino acid tryptophan via the kynurenine pathway[142]. Such *de novo* synthesis of niacin decreases with protein malnutrition, and deficiencies in Fe, riboflavin and pyridoxine[142,143]. South Africa has a long history of malnutrition, including micronutrient deficiencies[115]. From the reviewed literature, we can feasibly assume malnutrition, particularly malnutrition associated with maize as the staple in nutritionally inadequate diets, to be the main cause of pellagra.

Alcoholism may have been the second major cause of pellagra. Alcohol can cause or aggravate niacin deficiency by causing malnutrition, gastrointestinal disturbances, B vitamin deficiencies, and by suppression of *de novo* synthesis of niacin[144]. According to the WHO, South Africa has among the highest per capita alcohol consumption rates in the world[145]. According to the Institute for Health Metrics and Evaluation, alcohol ranked among the top three risk factors that accounted for the 2010 disease burden in South Africa[146]. In fact, alcohol consumption is a historical problem in South Africa. Between 1895 and 1909, the Natal Government Asylum, cited 'intemperance in drink' as the most frequently identified cause of insanity amongst male patients[147]. A 1942 study in the Transkei found that the much higher incidence of pellagra in the

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Pondomisi tribe, compared to the Fingo tribe, was due to a higher alcohol intake[23]. Pellagra, as well as suboptimal niacin levels, were linked to higher alcohol intake in Venda men[44,48]. In late 1970s, malnutrition and alcohol were implicated as causes of pellagra in admissions to psychiatric hospitals[123]. Pellagra has also been linked to alcohol consumption in dermatological patients visiting Baragwanath Hospital during 1969–1972[50]. In a 1984 overview of poverty and development in KwaZulu-Natal, a strong association is described between incidences of pellagra and alcoholism[61].

A number of drugs[148–150] may influence niacin levels, but most are probably not used on a scale that would significantly influence the local prevalence of pellagra, except anti-tuberculosis agents. South Africa has a high incidence of tuberculosis and HIV-tuberculosis co-infection. According to the WHO, about 57 % (258 000) of the 45 400 patients with incident tuberculosis in 2015 were HIV positive[151]. The anti-tuberculosis drug, isoniazid, interferes with the conversion of tryptophan to niacin by producing a deficiency in pyridoxine coenzymes required for *de novo* synthesis of niacin. Several authors have reported pellagra symptoms in patients treated with isoniazid, especially poorly nourished patients, and at least one paper called to the fact that pellagra encephalopathy may occur in patients without pellagra-associated skin lesions[152,153]. Niacin deficiency has occasionally been linked to HIV infection, and South Africa has a very high incidence of HIV. However, it is debatable whether niacin deficiency occurs as a result of HIV infection *per se* as the high pro-inflammatory activity associated with HIV infection stimulates *de novo* niacin synthesis at the cost of tryptophan levels[142]. Above normal *de novo*, niacin synthesis then scales down when the inflammatory activity normalises in response to anti-retroviral therapy[142]. Nevertheless, the niacin status of HIV-positive patients may be adversely affected by the malnutrition and malabsorption often observed in HIV-positive patients[154].

The end of pellagra or niacin deficiency in South Africa?

The prevalence of pellagra, as diagnosed by dermatological symptoms, declined with improvement in socio-economic conditions, food fortification, social grants and food security programmes. Despite numerous food security programmes, the prevalence of deficiencies in several other micronutrients remains unacceptably high[115]. Currently, most micronutrient deficiencies are diagnosed using biochemical assessments, often in the absence of their respective deficiency syndromes. In contrast, niacin deficiency is still mainly diagnosed based on dermatological symptoms of pellagra, disregarding potential subclinical deficiency. Niacin levels may even be kept within normal range by *de novo* synthesis, at the cost of tryptophan levels.

Although few papers reported incidences of pellagra in South Africa since the end of the 20th century, outbreaks have recently been reported in specific regions of neighbouring countries. Regrettably, admissions to a clinic at Kuito in the Bie Province of central Angola showed that the incidence of clinical pellagra has not decreased since the end of the civil war in 2002[155]. In Malawi, between July 2015 and April 2016, a total of 691 pellagrins were seen at a local Kasese catchment area clinic in Dowa. The clinic serves approximately 30 000 people, largely of the Chichewa tribe[156]. In central Mozambique, an outbreak of pellagra, following the March 2019 hit by *Cyclone Idai*, is reported to affect almost 4000 people in the Sofala and Manica provinces, with the numbers still increasing[157]. In Zimbabwe, 2007 pellagra cases were recorded by village health workers between January and October 2020 and the numbers are expected to increase as food insecurity intensify[158]. In Lesotho, pellagra is said to have been the most common dietary deficiency disease with 8600 cases in 1959[159]. By 1964, the numbers started to decline, but indications are that it never really disappeared[159].

Limitations

Very few of the early papers and records could be traced through structured literature searches and were only uncovered through electronic hand searches and in library and other archives. Despite enormous efforts to discover all credible records on incidences of pellagra in South Africa, we suspect that some must have been overlooked.

Conclusions

In South Africa, the prevalence of pellagra peaked after it was all but eradicated in the USA and Europe. Pellagra never reached the same peak levels reported for Europe and the USA. However, inadequate medical services in rural areas, and in the erstwhile Black reserves and homelands, probably contributed to underestimation of the prevalence. As elsewhere, pellagra occurred mainly in the disadvantaged and in South Africa was most prevalent in Black populations. As elsewhere, pellagra was often associated with maize as staple food. Malnutrition was the main cause, but excessive alcohol consumption contributed. Since 2000, only isolated cases of pellagra have been reported in South Africa. The absence of dermatological symptoms of pellagra does not exclude subclinical niacin deficiency.

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Supplementary material

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