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Alexander Oti Acheampong, Kwame Nkrumah University of Science and Technology School of Medicine and Dentistry, Kumasi Ghana, Collins Kokuro, Kwame Nkrumah University of Science and Technology School of Medicine and Dentistry, Kumasi, Ghana, Solomon Obiri-Yeboah, Kwame Nkrumah University of Science and Technology School of Medicine and Dentistry, Kumasi, Ghana, Frank Osei-Bonsu, University of Ghana School of Medicine and Dentistry, Accra, Ghana, Daniel Tormeti, University of Ghana School of Medicine and Dentistry, Accra, Ghana, Daniel Tormeti, University of Ghana School of Medicine and Dentistry, Accra, Ghana, Robert Nii Larmy Larmie, Komfo Anokye Teaching Hospital, Oral Health Directorate, Kumasi, Ghana, Nana Tuffour Ampem Gyimah, Komfo Anokye Teaching Hospital, Oral Health Directorate, Kumasi, Ghana, Clement Ani Obeng, Komfo Anokye Teaching Hospital, Oral Health Directorate, Kumasi, Ghana, Clement Ani Obeng, Komfo Anokye Teaching Hospital, Oral Health Directorate, Kumasi, Ghana, Bernard Puozaa, Komfo Anokye Teaching Hospital, Oral Health Directorate, Kumasi Ghana, Jonathan Karikari Mensah, Komfo Anokye Teaching Hospital, Oral Health Directorate, Kumasi Ghana, Samuel Baffour-Awuah, Komfo Anokye Teaching Hospital, Oral Health Directorate, Kumasi Ghana, Peter Donkor, Kwame Nkrumah University of Science and Technology School of Medicine and Dentistry, Kumasi Ghana.

Corresponding author: Dr. Collins Kokuro, Kwame Nkrumah University of Science and Technology, School of Medicine and Dentistry, UPO, Kumasi Ghana. Email: kokuro70@gmail.com

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A. O. Acheampong, C. Kokuro, S. Obiri-Yeboah, F. Osei-Bonsu, D. Tormeti, R. N. L. Larmie, N. T. A. Gyimah, F. Anarfi, C. A. Obeng, B. Pouzaa, J. K. Mensah, S. Baffour-Awuah and P. Donkor

ABSTRACT

Background: Severity of orofacial infections is dependent on a balance between host immunity and causative microbe related factors. Severe orofacial infections (SOI), if not controlled, could lead to serious complications.

Aim: The aim of this study was to determine the conditions associated with severe orofacial infections seen at the Komfo Anokye Teaching Hospital (KATH).

Materials and Methods: This was a 2-year retrospective study of all cases of orofacial infections admitted to the oral and maxillofacial surgery ward of KATH from January 2017 to December 2018. A specially designed form was used to collect relevant information from patients' records. Data was entered into Excel and later transported to SPSS for analysis. Ethical approval was obtained.

Results: A total of one hundred and twenty (120) patients were seen during the period comprising 75 males and 45 females, giving a male to female ratio of 1.6:1. Eighty-one (67.5%) of the patients had low haemoglobin levels at the time of admission and 11.7% were known hypertensives on medication while 10.3% were newly diagnosed cases of hypertension. 17.0% were known

diabetes mellitus (DM) patients and were on oral hypoglycemic agents but only 56.8% of them took their medication regularly. An additional 23.7% were newly diagnosed with DM. Sixty-four (64) has liver impairment, 79 had renal impairment.

Conclusion: Anemia was the major condition associated with the SOI. This meant that in the management of SOI, correction of anaemia should be prioritized. DM, uncontrolled hypertension, renal and liver diseases were also seen to be associated with SOI.

INTRODUCTION

Severe orofacial infections (SOI) are those that extend outside the alveolar process of the jaw, to involve adjacent anatomical spaces or cause marked trismus, swelling, or pain, with the patient's body temperature above 38°C according to Heimdahl et al(1). It is usually the end result of an initially long and slow disease process originating predominantly from dental caries, dental occlusal trauma leading to pulp necrosis, periodontal pockets and pericoronitis of partially erupted teeth(2,3).

Severity of orofacial infection is however dependent on balance between host immunity and causative microbe related factors(4). If not controlled, it may lead to complications respiratory such as obstruction, necrotizing fasciitis, mediastinitis, pleuritis, sepsis and cerebral abscess, due to the ability of causative organisms to spread to contigious fascial spaces and hematogenously to distant sites(4–7).

In a South African study by Molomo et al, 57.9% of those affected with SOI were males with an average age of 38.62 years(8). Santosh et al, also reported that males were more prone to odontogenic space infections compared to females(9). There were similar findings in studies done in Nigeria, United State of America and India with males being more affected than females(10–12).

Whilst Bahl et al. reported the mandibular 3rd molar as most common offending tooth followed by the mandibular 2nd molar(12), Santosh et al, reported mandibular first molar as the most common offending tooth followed by the mandibular 2nd molar, maxillary first molar and mandibular third molar(9). Adetayo et al and Sanchez et al, however reported that lower posterior teeth were the most common sources of orofacial infections(13,14).

The submandibular space was reported as the most commonly involved fascial space in both single- and multiple- space infections(11,12). However, other investigators such as Patankar et al. and Santosh et al. reported that maxillary teeth were the predominant source of orofacial infections with the buccal space being the most commonly involved(9,15).

Studies done by Ugboko et al. and Sanchez et al. revealed diabetes mellitus as the comorbidity with the highest incidence in patients with Ludwig's angina(10,14). Bahl et al. also reported diabetes mellitus and hypertension as systemic diseases with the highest occurrence (10.0% each) in patients with orofacial infections compared to HIV (1.0%)(12).

Heimdal et al. as well as Konown at al. found that white blood cell count (WBC) is of minor importance in determining the severity of orofacial infections, as there were no significant differences in the mean values of WBC count in both mild and severe infections(1,3).

The mainstay of management of severe orofacial infection combines antibiotic therapy and surgical intervention including decompression through incision and drainage and elimination of the source of the infection(12,16). Adetayo et al believe serial surgical debridement plays a very important role in successful management in patients with severe orofacial infections(13). Culture and sensitivity results are imperative for the successful management in case there is resistance to empirical antibiotic treatment(8).

In a 5-year review of odontogenic infections in the largest Teaching Hospital in Ghana, Accra, it was reported that severe odontogenic infections had a fatality rate of 5.8%(17).

The aim of this study was to determine the conditions associated with severe orofacial infections seen at the oral and maxillofacial surgery unit of the Komfo Anokye Teaching Hospital.

MATERIALS AND METHODS

This was a 2-year retrospective study of all cases of orofacial infections admitted to the oral and maxillofacial surgery ward of KATH from January 2017 to December 2018. A data capturing form was designed and relevant information from patients' medical records were collected. The information gathered included age, sex, history of presenting complaint, medical and surgical history, offending agent, laboratory results, treatment and outcome. Data was first entered in Excel and later transported to SPSS version 20 (SPSS, Inc. Chicago Illinois) after editing and cleaning for analysis. Qualitative data was shown as percentages while quantitative data were summarized by their mean, standard deviation, range and percentiles.

Ethical approval was obtained from the Committee on Human Research and Publication Ethics (CHRPE) of Kwame Nkrumah University of Science and Technology/Komfo Anokye Teaching Hospital.

Anemia was classified as follows: Mild anemia (Hb level 11.9 - 10g/dl), Moderate anemia (Hb level 9.9 - 7g/dg) and Severe anemia (Hb level less than 7g/dl)(18).

Hypertension was defined according to World Health Organization (WHO) criteria(19). Patients were diagnosed to have hypertension if systolic blood pressure, SBP was \geq 140 mm Hg and/or diastolic blood pressure, DBP \geq 90 mm Hg, or patient was taking anti-hypertensive medications as documented in their medical records. Diabetes mellitus was defined according the World Health Organization (WHO) criteria (20).

RESULTS

A total of hundred and twenty (120) patients with SOI were seen during the two-year period which was made up of 75 males and 45 females. The male to female ratio was 1.7:1.

ID	Patient characteristic (N=120)		
Average age in yrs (range) [T]	44.3 (15-87)		
F	46.6		
Μ	40.5		
A ! . I			
Associated condition	Number of patients n (%)		
Associatea condition Anemia [T]	Number of patients n (%) 81 (67.5)		
	÷		
Anemia [T]	81 (67.5)		

 Table 1:

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Neutrophilia [T]	65 (54.2)
F	45 (69.2)
Μ	20 (30.8)
Hypertension [T]	26 (21.7)
Known before admission	14 (11.7)
Not previously known	12 (10.0)
Diabetes Mellitus [T]	49 (40.8)
Known before admission	20 (16.6)
Not previously known	29 (24.2)

n= number of subjects, F=females, M=males, T=total, yrs=years

From Table 1.0, the average age was 44.3 years and age range was 15 to 87 years. For males, the average age was 46.6 years.

At the time of admission, 11.7% were known hypertensives and 10.0% were first diagnosed of hypertension at the time of admission, making a total of 21.7% hypertensives. Also 16.6% confirmed they were diabetic and an additional 24.2% were diagnosed on the ward. All those known cases of DM were on oral hypoglycemic but only 56.8% were compliant with their medication. Forty percent (0.0%) of the DM patients also had mild renal impairment while 12.7% had severe liver impairment. 54.2% of the patients had neutrophilia with the majority being female.



Figure 1.0 Proportion of offending tooth in Severe orofacial infections (SOI)

All the SOI were of odontogenic origin. Eighty-eight percent (88.4%) occurred in the mandible while 11.6% occurred in the maxilla. The proportions of offending teeth in decreasing order were as follows: first mandibular molars (40.0%), third mandibular molar (29.2%), second mandibular molar (19.2%), first maxillary molar (8.3%), maxillary canine (3.3%) as shown in Figure 1.0.

Mortality of 5% was recorded with a 2:1 male to female ratio. Four of the mortalities had both DM and hypertension, severe liver impairment, mild renal failure. They had all

defaulted in their medications (antihypertensive and hypoglycemic) prior to admission for the orofacial infections. The remaining two mortalities had severe liver impairment from liver malignancy. Additional hematological, liver function tests, kidney function tests are represented in the Tables below:

ID	Mild (n)	Moderate (n)	Severe (n)	Total n (%)
Т	19	55	7	81 (67.5)
F	15	25	5	45 (55.6)
M	4	30	2	36 (44.4)
Average Hb(mg/dl)	10.09	8.08	6.63	8.43

Table 2		
Relationship between gender and severity of anemia among patients with SOI		

n= number of subjects, F=females, M=males, T=total, Hb= haemoglobin levels, yrs=years.

According to Table 2.0, over sixty seven percent of the patients seen had low haemoglobin level at the time of admission of which 45(55.6%) were females and 36(44.4%) males. Majority of the patients with anemia had moderate anemia. The average age of patients with mild, moderate and severe anemias were 47, 60 and 53 years respectively.

Table 3				
Three major abnormal biochemical parameters of patients with SOI				

Biochemical parameter	Females n (%)	Males n (%)	Total n (%)
Liver impairment	35 (54.7)	29 (45.3)	64 (53.3)
Renal impairment	27 (34.2)	52 (65.8)	79 (65.8)
Fasting hyperglycemia	26 (63.4)	15 (36.6)	41 (34.2)

N=120, Average FBS=12.7mmol/L, Average age for liver impairment=32yrs, Average age for renal impairment = 53yrs, Average age for fasting hyperglycemia=50yrs

From Table 3.0, a total of 64 patients had liver impairment, making 53.3% of all patients. Majority were females, 54.7%. Twenty-three percent (23.3%) of the patients had severe liver impairment. Seventy-nine (79) patients had renal impairment, making 65.8% of all patients. Majority of patients with renal impairment were males. Again, from Table 3.0, 34.1% had high blood sugar level at the time of admission. There were more females (63.4%) with hyperglycemia than males (36.6%).



Figure 2.0. A. Patient with odontogenic infection presenting with raised tongue. B. Patient presenting with facial cellulitis and raised tongue secondary to odontogenic infection. C. Old lady with necrotizing fasciitis. Note the application of herbal medicines on the swelling. D. Extension of odontogenic infection to the chest and left breast.



Figure 3.0. A.B.C.D. Shows different patients showing various degrees of necrotizing fasciitis secondary to odontogenic infection. D. shows a patient with necrotizing fasciitis after initial wound debridement has been done.

DISCUSSION

In this present study involving 120 patients with SOI, majority were males and the average age was 44.3 years. This finding is similar to some studies in Nigeria, South Africa, India, United States of America, and South America such as a study done in South Africa by Molomo et al, where 57.9% of those affected were males with an average age of 38.6 years(8,10–12). Santosh et al, also reported that males were more prone to odontogenic fascial space infections compared to females(9). This phenomenon may imply that either males don't pay as much attention to their oral health or visit the dentist less or probably late. In a study conducted by Manski et al it was reported that females visited dentists regularly and had better oral hygiene compared to males(21).

The mandible was the commonest jaw affected with SOI and the first mandibular molar tooth was the most common source of odontogenic infection in this study. This is probably due to the fact that it erupts early and at a time when the individual is not skilled enough for optimal oral health care(12). This was consistent with other findings by other researchers such as Santosh et al(9). By contrast, , Bahl et al. reported that mandibular 3rd molar was most common offending tooth followed by mandibular 2nd molar(12).

The lower molar teeth are known to cause SOI because their root apices are located above the mylohyoid muscles. This enables infections to easily spread to the sublingual and submental spaces before the submandibular spaces(22).

In this present study, it was evident that over 40% of all SOI cases presented with DM, making the condition one of major predisposing factors as illustrated in Tables 1.0 and 3.0. There was of a higher proportion of patients with DM compared to the study by Bahl et al, however, our findings were consistent with those of Whiteside et al which recorded over 45% of the patients with DM(12,23).

An important observation we made was that majority of the DM cases were only diagnosed at the time of admission. This could have worsened and embarrassed the host immunity making them susceptible to SOI. It is a known fact that uncontrolled DM patients may have suppressed immunity due to impairment in leucocyte function and a high glycemic state is good ground for infections to thrive in any part of the body(24) including the orofacial region, hence the predisposition to SOI. Hypertension was recorded in 21.7% of all the admitted cases of SOI (Table 1). This is similar to other studies from the subregion(10,13).

The major significant condition among the cases in this study was that, over 65.0% had anemia at the time of admission on the ward (Tables 1.0 and 2.0), making anemia a major predisposing factor in SOI. Adequate haemoglobin is needed for the survival of cells including the ability to prevent and mount enough defense to fight infection. Lower haemoglobin levels affect recovery

from infections in all organ systems including odontogenic infections. Anemia leads to general body weakness, tiredness and lowered resistance to diseases including infections(25,26). Anemia can thus cause immunosuppression making the individual susceptible to SOI.

Nearly half of the patients had neutrophilia which is similar to studies by Heimdahl et al and Konown et al even though they all reported that white blood cell count is of minor importance in determining the severity of orofacial infections(1,3).

It can only be speculated from this study that, low haemoglobin, the presence of DM and high blood pressure further weakens the immunity of the individual to become susceptible to SOI.

It is well-known that renal impairment result could from uncontrolled hypertension(27) and renal impairment is a risk factor for infections. Approximately 30% of Ghana's population are affected by non-alcoholic fatty liver disease (NAFLD) and this can cause significant liver disease in significant proportion of patients, according to a study done by Agyei-Nkansah(28). Renal and liver disease are becoming a major public health issues in Ghana(28–30), and could further compromise the immunity of the host and thus predispose them to SOI. In this study, majority of the patients had renal and liver dysfunction (Table 3.0). Since the mainstay of treatment after surgery for SOI is medical, there is a significant use of antibiotics. Many of the antibiotics used in SOI can potentially harm the kidneys and liver and these risks are even more pronounced in patients with accompanying impairment of liver and or renal function. For example, penicillin may cause renal impairment; Clavulanic acid may cause liver impairment in the elderly; Metronidazole in high doses can cause renal and liver impairment; Gentamycin is also potentially nephrotoxic. All these are the backbone of empiric antibiotics used in the management of SOI. The choice of antibiotics used in SOI therefore should be influenced by their side effects and potential toxicity and their effect on the kidney and liver. The baseline renal and liver functions therefore must be checked and taken into account in the choice of antibiotics.

Limitation of study: This study did not determine the severity of the SOI using C-Reactive Protein which could have shown how these predisposing conditions impacted on the severity of SOI. Data on culture and sensitivity was also not available and we recommend that it be included in a future study to help determine how the predisposing factors influence the type of organism and the choice of antibiotics. Being a retrospective study, the available data could also not give us information about the type of anemia. Further prospective study is needed to ascertain the exact relationship between SOI and the associated conditions.

CONCLUSION

Anemia was a major predisposing factor in the SOI. This meant that in the management of SOI, a full blood count is very important so clinicians can determine the type of the anemia for the right hematinic to be administered. Diabetes mellitus, uncontrolled hypertension, renal and liver diseases were also seen to be associated with SOI. These conditions probably compromise the immunity of the host which facilitates the progression of a simple tooth infection into SOI.

RECOMMENDATION

It is known that culture and sensitivity testing are very important in the management of SOI so that appropriate antibiotics are selected. Investigations to determine the presence of the abovementioned associated conditions are equally important. These conditions should also be managed to strengthen the immunity of the host for better outcomes of the management of SOI.

REFERENCES:

1. Heimdahl A, von Konow L, Satoh T, Nord CE. Clinical appearance of orofacial infections of odontogenic origin in relation to microbiological findings. J Clin Microbiol [Internet]. 1985;22(2):299–302. Available from: http://www.ncbi.nlm.nih.gov/pubmed/4031041

2. Huang T-T, Liu T-C, Chen P-R, Tseng F-Y, Yeh T-H, Chen Y-S. Deep neck infection: analysis of 185 cases. Head Neck [Internet]. 2004;26(10):854–60. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15390207

3. Konown L von, Nord CE. Ornidazole compared to phenoxy methylpenicillin in the treatment of orofacial infections. J Antimicrob Chemother [Internet]. 1983 Dec 9;11(3):207–15. Available from:

https://academic.oup.com/jac/article/11/3/207/784 004

4. Jiménez Y, Bagán JV, Murillo J, Poveda R. Odontogenic infections. Complications. Systemic manifestations. Med Oral Patol Oral Cir Bucal [Internet]. 2004;9 Suppl:143. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/15580132 5. Bounds GA. Subphrenic and mediastinal abscess formation: a complication of Ludwig's angina. Br J Oral Maxillofac Surg [Internet]. 1985;23(5):313–21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/2932142

Wang J, Ahani A, Pogrel MA. A five-6. year retrospective study of odontogenic maxillofacial infections in a large urban public hospital. Int J Oral Maxillofac Surg [Internet]. 2005 Dec 9;34(6):646-9. Available from: http://www.sciencedirect.com/science/article/pii/ S0901502705000822

7. Mumtaz R, Arain A, Suhail A, Rajput S, Adeel M, Hassan N. Deep neck space infections; retrospective review of 46 patients [Internet]. Journal of Cranio-Maxillary Diseases. 2014. Available from: https://link.galegroup.com/apps/doc/A365007774

/AONE?sid=lms

8. Molomo E, Motloba P, Bouckaert MM, Tlholoe MM. Bacteriology and management of orofacial infections in a Maxillofacial and Oral Surgery Clinic, South Africa. J Dent Assoc S Afr [Internet]. 2016;71:474–7. Available from: https://www.researchgate.net/publication/317449 061_Bacteriology_and_management_of_orofacial _infections_in_a_Maxillofacial_and_Oral_Surger y_Clinic_South_Africa

9. Santosh AN, Viresh AN, Sharmada BK. Microbiology and Antibiotic Sensitivity of Odontogenic Space Infection. Int J Med Dent Sci [Internet]. 2014 Dec 9;3(1):303–13. Available from:

http://informaticsjournals.com/index.php/ijmds/a rticle/view/19408

10. Ugboko V, Ndukwe K, Oginni F. Ludwig's angina: an analysis of sixteen cases in a suburban Nigerian tertiary facility. African J Oral Heal [Internet]. 2005 Dec 9;2(1–2). Available from:

https://www.ajol.info/index.php/ajoh/article/vie w/56993

11. Kim MK, Chuang S-K, August M. Antibiotic Resistance in Severe Orofacial Infections. J Oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg [Internet]. 2017;75(5):962–8. Available from:

https://www.joms.org/article/S0278239116310977 /pdf

12. Bahl R, Sandhu S, Singh K, Sahai N, Gupta M. Odontogenic infections: Microbiology and management. Contemp Clin Dent [Internet]. 2014 Dec 9;5(3):307–11. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC 4147804/

13. Adetayo A, Oyedele T, Sodipo BO, Olawale E, Ajimoko AO, Somoye MS. Management of severe orofacial infections: Report of two cases and literature review. Int J Infect Trop Dis [Internet]. 2017;4:18–27. Available from:

https://www.researchgate.net/profile/Titus_Oye dele/publication/317683788_Management_of_sev ere_orofacial_infections_Report_of_two_cases_a nd_literature_review/links/596f28540f7e9bd5f763 be20/Management-of-severe-orofacial-infections-Report-of-two-cases-and-l

14. Sánchez R, Mirada E, Arias J, Paño J-R, Burgueño M. Severe odontogenic infections: epidemiological, microbiological and therapeutic factors. Med Oral Patol Oral Cir Bucal [Internet]. 2011;16(5):e670-676. Available from: https://doi.org/10.4317/medoral.16995

15. Patankar A, Dugal A, Kshirsagar R, Hariram, Singh V, Mishra A. Evaluation of microbial flora in orofacial space infections of odontogenic origin. Natl J Maxillofac Surg [Internet]. 2014 Dec 9;5(2):161–5. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC 4405958/

16. Flynn TR, Shanti RM, Levi MH, Adamo AK, Kraut RA, Trieger N. Severe odontogenic infections, part 1: prospective report. J Oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg [Internet]. 2006;64(7):1093–103. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/16781343

17. Blankson PK, Parkins G, Boamah MO, Abdulai AE, Ahmed AM, Bondorin S, et al. Severe odontogenic infections: A 5-year review of a major referral hospital in Ghana. Pan Afr Med J [Internet]. 2019 [cited 2020 Apr 9];32:71. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/31223362

18. WHO | Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity [Internet]. WHO. 2019. Available from: http://www.who.int/vmnis/indicators/haemoglo bin/en/

19. Chalmers J, MacMahon S, Mancia G, Whitworth J, Beilin L, Hansson L, et al. 1999 World Health Organization-International Society of Hypertension Guidelines for the Management of Hypertension. Clin Exp Hypertens [Internet]. 1999 Dec 16;21(5–6):1009–60. Available from: http://www.tandfonline.com/doi/full/10.3109/106 41969909061028

20. WHO. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Part 1, Diagnosis and classification of diabetes mellitus. 1999 Dec 16; Available from: https://apps.who.int/iris/handle/10665/66040

21. Manski RJ, Macek MD, Moeller JF. Private dental coverage: Who has it and how does it influence dental visits and expenditures? J Am Dent Assoc [Internet]. 2002 Dec 10;133(11):1551–9. Available from: http://www.sciencedirect.com/science/article/pii/ S0002817714646201 22. Kaluskar S, Bajaj P, Bane P. Deep space infections of neck. Indian J Otolaryngol Head Neck Surg. 2007;59(1):45–8.

23. Whitesides L, Cotto-Cumba C, Myers RA. Cervical necrotizing fasciitis of odontogenic origin: a case report and review of 12 cases. J Oral Maxillofac Surg Off J Am Assoc Oral Maxillofac Surg [Internet]. 2000;58(2):144–51; discussion 152. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10670592

24. Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: A review of pathogenesis. Indian J Endocrinol Metab [Internet]. 2012 Dec 16;16(Suppl1):S27–36. Available from: https://www.ncbi.plm.pib.gov/pmc/articles/PMC

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC 3354930/

25. Sharmanov A. Anaemia in Central Asia:
Demographic and Health Survey Experience.
Food Nutr Bull [Internet]. 1998 Dec 16;19(4):307–
17. Available from: https://doi.org/10.1177/156482659801900405

26. Taylor M, Jinabhai CC, Couper I, Kleinschmidt I, Jogessar VB. The effect of different anthelmintic treatment regimens combined with iron supplementation on the nutritional status of schoolchildren in KwaZulu-Natal, South Africa: a randomized controlled trial. Trans R Soc Trop Med Hyg [Internet]. 2001 Dec 16;95(2):211–6. Available from: http://www.sciencedirect.com/science/article/pii/ S0035920301901713

27. Vidal-Petiot E, Metzger M, Faucon A-L, Boffa J-J, Haymann J-P, Thervet E, et al. Extracellular Fluid Volume Is an Independent Determinant of Uncontrolled and Resistant Hypertension in Chronic Kidney Disease: A NephroTest Cohort Study. J Am Heart Assoc [Internet]. 2018;7(19):e010278. Available from: https://www.ahajournals.org/doi/pdf/10.1161/JA HA.118.010278

28. Agyei-Nkansah A. Mitigating the scourge of non-alcoholic fatty liver disease in Ghana. Ghana Med J [Internet]. 2017 Dec 10;51(3):98–100. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC 5870229/

29. Ephraim RK, Biekpe S, Sakyi SA, Adoba P, Agbodjakey H, Antoh EO. Prevalence of chronic kidney disease among the high risk population in South-Western Ghana; a cross sectional study. Can J Kidney Heal Dis [Internet]. 2015;2:40. Available from: https://europepmc.org/articles/pmc4630826?pdf= render

30. de-Graft Aikins A. Ghana's neglected chronic disease epidemic: a developmental challenge. Ghana Med J [Internet]. 2007 Dec 10;41(4):154–9. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC 2350116/