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EDITORIAL

RESIDENCY TRAINING: BRIDGING THE GAP BETWEEN MEDICINE AND DENTISTRY

Dentistry has long been perceived as a specialised branch of medicine and is often viewed in isolation from broader healthcare. However, emerging research and clinical experience increasingly highlight the essential role of oral health in systemic well-being.

The mouth is often described as a mirror of systemic health, with oral findings frequently providing early indicators of conditions such as diabetes, cardiovascular disease, and autoimmune disorders. Periodontal disease has been strongly linked to an increased risk of atherosclerosis and adverse pregnancy outcomes. Similarly, xerostomia (dry mouth) may signal underlying conditions like Sjögren's syndrome or be a side effect of commonly prescribed medications. Poor oral health can also contribute to medical complications such as endocarditis, pneumonia, and adverse pregnancy outcomes. Therefore, these strong interrelated connections will require some integration of dental education into medical residency programs to improve patient outcomes, foster interdisciplinary collaboration, and enhance healthcare delivery.

Currently, with the exception of the family medicine speciality, most residency programs in Ghana offer very little to no dental education in their medical residency program. It may be time to look again at this "Mouthless" Medical residency training and bridge the gap both in the curriculum and in practice. By incorporating dental education into residency programs, physicians will be better prepared to recognise and if not manage, refer patients with oral-systemic conditions to get the necessary and needed care.[1,2] This gap in education often leads to

- Missed Diagnoses: Physicians may fail to recognise early signs of oral conditions that could have serious consequences if left untreated, and that can also compromise the treatment being provided.
- Limited preventive guidance: Physicians are in a prime position to educate patients about disease prevention and oral hygiene, but without training, they may not prioritize these discussions.
- Inappropriate antibiotic use: Without proper training, medical residents may prescribe antibiotics unnecessarily for dental infections, contributing to antibiotic resistance

Beyond individual patient care, dentistry also plays a crucial role in public health. The increasing burden of non-communicable diseases, including oral cancers, periodontal disease and dental caries, calls for a more integrated approach to prevention and education. Fluoride programs, HPV vaccination campaigns to prevent oropharyngeal cancers, and early screening initiatives exemplify how dentistry contributes to broader health strategies.

Sheiham *et al*,[3] in advocating for a common risk factor approach in promoting oral health, argues that conventional oral health education is not effective nor efficient. Many oral health programmes are developed and implemented in isolation from other health programmes which often leads, at best, to a duplication of effort, or worse, conflicting messages being delivered to the public. He makes a case that since most of these oral conditions share common risk factors for a number of other chronic diseases, adopting a collaborative approach is more rational than one that is disease-specific. If this approach is highlighted also in our medical residency training, our health promotion programs may be more holistic and effective. Additionally, oral health disparities remain a pressing concern, particularly among underserved populations. Addressing these inequities requires interdisciplinary collaboration and policy-driven solutions.

By bridging the gap between medicine and dentistry during residency training, healthcare providers can work together more effectively to provide comprehensive patient care. By integrating dental training into residency programs, physicians will be better equipped to address oral health concerns, leading to improved patient care and more effective disease prevention.
Furthermore, healthcare is increasingly moving toward interdisciplinary models where different specialities work together to provide holistic patient care. However, the separation of medicine and dentistry remains a significant barrier. Training medical residents in dentistry can foster better collaboration between physicians and dentists by:

Encouraging Cross-Referrals: When physicians understand the importance of oral health, they are more likely to refer patients to dentists for timely intervention.
Improving Communication: Shared training experiences can help physicians and dentists develop a common language, making it easier to coordinate care for complex cases.

Enhancing Team-Based Care: Hospitals and clinics that integrate oral health into their medical teams see better patient outcomes, particularly for populations with high rates of oral disease, such as the elderly, diabetic patients, and those undergoing cancer treatment.

Strategies to incorporate Dental Training in Medical Residency Programs

Several strategies can be used to incorporate dental education into medical residency training:

- Integrated Curriculum: Residency programs should introduce mandatory coursework on oral health, covering topics such as oral infections, dental

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trauma, and the impact of chronic diseases on the mouth.

- Oral Health Rotations: Medical residents, especially those in primary care, emergency medicine, paediatrics and internal medicine, should complete rotations in dental clinics or hospital-based dental departments.
- Interdisciplinary Grand Rounds: Hospitals should hold joint case discussions involving both medical and dental professionals to improve collaborative problem-solving.
- Simulation Training: Using patient simulators, residents can learn to recognize and manage common oral health conditions, such as abscesses, ulcers, and oral manifestations of systemic diseases.

By incorporating these strategies into residency training, medical professionals will be better prepared to help address oral health concerns in their patients.

Conclusion

Oral health is a critical component of overall health, a siloed approach to healthcare provision can lead to fragmented patient care. Postgraduate medical training programs should integrate core dental concepts, particularly for specialities such as internal medicine, paediatrics, cardiology, endocrinology, and geriatrics. A collaborative model, where physicians and dentists co-manage medical conditions, can significantly enhance patient care. By integrating dental training into residency programs, physicians can develop a more comprehensive understanding of oral-systemic connections, leading to better patient care and stronger partnerships between medicine and dentistry. These may be achieved through joint training programs, research initiatives, or integrated clinical pathways. By doing so, we can break down the barriers between these disciplines and create a healthcare system that truly prioritizes holistic patient well-being. As healthcare continues to evolve toward a more holistic, team-based approach, embracing this synergy and closing the gap between medicine and dentistry will be essential for advancing comprehensive, patient-centred care and improving outcomes.

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ORIGINAL ARTICLES

ASSESSMENT OF ANTIBIOTIC RESISTANCE IN *STREPTOCOCCUS* ISOLATES CAUSING INFECTION OF THE ORAL CAVITY IN COVID-19 RECOVERED PATIENTS

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Abstract

Objective: This study evaluates the load of *Streptococcus* species and assesses their antibiotic resistance in COVID-19-recovered patients (Group A) and healthy patients (who never suffered from COVID-19, Group B) attending the out-patient department in tertiary care dental hospital in Bhubaneswar, Odisha.

Methodology: Unstimulated saliva samples were collected from 25 patients of each group and were screened for *Streptococcus* species. Further species-level identification was done using routine microbiological, biochemical, antigen-detection kits, and PCR techniques. The antibiotic sensitivity test was carried out using the Kirby-Bauers disk diffusion test.

Results: Five different species of *Streptococcus* were isolated. In both groups, *Streptococcus mutans* isolates were more in number, followed *by S. pyogenes*. Our study also recorded that the *Streptococcus* strains isolated from COVID-19-recovered patients were resistant to more antibiotics than those isolated from non-COVID patients.

Conclusion: In conclusion, there has been a significant rise in the MDR strains of *Streptococcus* species in India and globally. In our study, COVID-19-recovered patients had more *Streptococcus* species isolated from their oral cavity than strains isolated from the healthy controls. Hence, dental hospitals and clinics can implement modified safety regulations and antibiotic policies to reduce infections and antibiotic resistance problems.

Key words: *Covid 19; Streptococcus species; Antibiotic resistance; Oral infections; Oral Microbiome.*

Introduction

The SARS-CoV-2 infection, originally started in Wuhan, China, in December 2019, has resulted in several post-COVID-19 clinical complications. This pandemic also warned of giving rise to several opportunistic co-infections among COVID-19-infected individuals[1]. The coronavirus mainly affected the oropharyngeal region of COVID-19 patients, adversely affecting this region and disturbing the oral microbiota. The oral cavity is a reservoir of 700 species of normal flora and the central portal of entry of microbial pathogens. *Streptococcus* species are the most prevalent one around the oropharyngeal region in the human body and can invade easily [2,3]. Though *Streptococcus* is one of the oldest inhabiting bacteria in human beings, these pathogens invade and proliferate, which may result in dental caries and other periodontal conditions [4,5]. As a result, antibiotics were widely provided to COVID-19 patients even though antibiotics are useless against viruses such as COVID-19. Almost 80% of individuals hospitalized with COVID-19 received antibiotics in some manner [6,7]. The escalation of antibiotic resistance in *Streptococci* has been associated with several mechanisms, including efflux pumps and antimicrobial target modifications. Antibiotic resistance emerges from previously sensitive populations of *Streptococci* due to horizontal gene transfer or chromosomal point mutations caused by antimicrobial overuse. *Streptococci* strains are also known to produce biofilms. Increased antibiotic resistance of *Streptococci* biofilms promotes persistent infection, accounting for approximately 80% of human microbial infections [8,9]. Therefore, there have been concerns that increased antibiotic use (both prescribed and unprescribed) to treat secondary infections associated with COVID-19 has led to antibiotic resistance among these normal flora and incoming pathogenic bacteria; however, direct evidence has been lacking [10,11]. Hence, assessing a load of *Streptococcal* infection and their response to antibiotic treatments in both COVID-19-recovered patients and non-COVID patients (patients who never tested positive) becomes essential. While the influence of COVID-19 pandemic on drug-resistant bacteria is yet unknown, it is apparent that there will be a shifting set of global threats to antibiotic resistance [12-16].

Numerous studies have been conducted on *Streptococcal* infections and their antibiotic resistance among various health groups. However, this study will be the first to check the occurrence of *Streptococcal* infections among COVID-19-recovered patients and its oral manifestation among them. Further, this study intends to check the load of *Streptococcus* species and assess their level of antibiotic resistance from COVID-19-recovered patients and healthy patients (who never

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suffered from COVID-19) attending the OPD in tertiary care dental hospital in Bhubaneswar, Odisha.

Materials and Methods

Study design

A hospital-based cross-sectional study was conducted among COVID-19 recovered (Group A) patients and non-COVID-19 patients (Group B, never diagnosed with COVID-19) visiting OPD of a tertiary care dental hospital in Eastern India, from March 2023 for Oral health conditions. The demographic and clinical data of the patients were documented in Excel sheets.

Ethical Permission

This study was carried out after the approval of the Institute Ethical Committee of the Dental Sciences via letter no. IEC-IDS/IDS.SOA/2023/I-41 dated 10th October 2023.

Sampling Method

A simple random probability sampling technique was used for the regular patients visiting the OPD of a tertiary care dental hospital in Bhubaneswar, Odisha. Fifty saliva samples (25 from COVID-recovered patients and 25 from non-COVID patients) were collected from the periodontal pocket and tested for antibiotic sensitivity.

Inclusion Criteria

i. COVID-19-recovered patients diagnosed with *Streptococcus* infections
ii. Non-covid-19 patients diagnosed with *Streptococcus* infections

Exclusion Criteria

i. Patients with multiple oral infections

Sample Collection

2 ml of unstimulated saliva was collected from the selected patients and immediately transferred to the sterile holding medium. Saliva samples mixed with holding medium were kept at room temperature, and then 2 ml of fresh 2 ml sample mixture was mixed with 8 ml of sterile normal saline and shaken to form a homogenous mixture. All samples were mixed by vigorous shaking and serially diluted.

Processing of Samples for Microbiological and Biochemical Investigations

All the samples were taken to the Central Research Laboratory, IDS, for further processing. Bacteria were incubated overnight at 37°C on blood agar plates for 24 h. The colonies formed on the plate were subjected to gram staining, routine microbiological and biochemical test for identification. Later, *Streptococci* species was confirmed using molecular biology method[17].

Microbiological Identification

The initial procedure involves conducting a Gram stain on the specimen. *Streptococci* are a type of Gram-positive cocci that exhibit a purple colouration when observed via a microscope. In addition, *Streptococci* are frequently categorized according to their capacity to induce lysis of erythrocytes on blood agar plates. This phenomenon is called hemolysis and can be classified into three distinct types: Alpha-hemolysis, Beta-hemolysis, and Gamma-hemolysis. *Streptococci* have a catalase-negative characteristic, indicating their lack of enzyme catalase production. Adding a small quantity of hydrogen peroxide to a colony on a slide results in the absence of bubble formation, indicating that the organism is catalase-negative. For sugar fermentation tests, a pure culture's inoculum is aseptically transferred to a sterile tube with phenol red sucrose broth. The inoculation tube is incubated at 35-37°C for 24 hours, after which the results are assessed. A positive test is characterized by a transition in hue from red to yellow, which signifies a shift in pH toward acidity [17, 18].

Antigenic Detection of Streptococcal Groups

The *Streptococca*l groups A, B, C, D, F, G, and H were efficiently identified using the process of latex agglutination, utilizing the Streptococcal Grouping Kit (Himedia, Mumbai). The primary objective of this quick latex agglutination test was to provide straight forward and expeditious outcomes for the detection and classification of *Streptococcal* groups A, B, C, D, F, G and H. The test employs latex particles coated with antibodies specific to a particular group. These antibodies clumped together when they got exposed to homologous antigens[18].

PCR Identification

The universal PCR performed with 50µl DNA sample was extracted from dental carries in a total reaction volume of 25 µl, consisting of 12 µl of master mix, 1µl of forward primer, 1 µl of reverse primer,3µl of DNA sample, and 8 µl of molecular grade water. PCR was carried out with a semiquantitative thermal cycler under the following conditions: initial denaturation 95 °C for 10 min, denaturation 94 °C for 2 min, annealing 55-60 °C for 30 sec, and then extension 72 °C for 45 sec and then repeat the three cycles 30 times and then final extension 72 °C 10 min. To detect the PCR product, 10 µl of amplified DNA was run on a 1% agarose gel with dye and ethidium bromide and visualized under UV light. DNA was isolated using a DNA isolation Kit (HiMedia, Mumbai) through agarose gel electrophoresis. 16S rDNA amplified with universal primer pairs 27F, 1525R (A); 27F, 1492R (B) and 530F, 1525R (C). Amplified genes were identified by comparison with 16S rRNA databases [19].

Antibiotic Sensitivity Test

All identified strains were subjected to antibiotic sensitivity tests by Kirby-Bauer's using a 4 mm thick blood agar/Muller Hinton agar. An aliquot of 0.1 mL of the exponentially growing culture was spread on agar for lawn development at 37°C in an incubator. Further, on the lawn-agar of each plate, eight antibiotic discs

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(HiMedia, Mumbai) were placed at equal distances from one another. Plates were incubated for 18 h at 37°C. The zone of inhibition around each antibiotic disk was measured and compared to the standard antibiotic susceptibility test chart of Clinical Laboratory Standard Institute guidelines[20].

The results were similar to *S. mutans* and *S. salivarius.* Further, *S. mitis* is gram-positive cocci with gamma-hemolytic colonies and is catalase-negative. Lastly, *S. pyogenes* was gram positive with beta-hemolytic colonies (Table 1).

Table 1. Gram staining, hemolytic, sugar fermentation, and antigenic detection test results of isolated different *Streptococcus* species

Isolated bacteria	Gram Stain	Colony characters on Blood Agar	Colony characters on Nutrient agar	Hemolysis	Sugar fermentation test		Antigenic Detection *Streptococcal* Groups
					Positive	Negative	
S. sanguis	+ve cocci	Glossy, round, translucent colonies	Glossy, round, translucent colonies	α	Lac, Raf, Tre	Man, Sor, VP	Group H
S. mitis	+ ve cocci	Round, grey, elevated, small colonies	Round, colorless/non-pigmented convex colonies	α	Lac	Man, Raf, Sor, Tre, VP	Viridans
S. mutans	+ ve cocci	Round, grey, elevated, small colonies	Round, greyish-white, elevated, small colonies	α	Man, Lac, Raf, Sor, Tre, VP		Group A
S. salivarius	+ ve cocci	Round, convex, white mucoid colonies	Round, convex, white butyrous colonies	α	Lac, Raf, Tre	Man, Sor, VP	Viridans
S. pyogenes	+ ve cocci	Round, Pinpoint, opaque Light yellow/off-white, matt colonies	Round, Pinpoint, opaque Light yellow/off-white, matt colonies	β	Lac, Tre	Man, Raf, Sor, VP	Group A

Note: Man: Mannitol, Lac: Lactose; Raf: Raffinose; Sor: Sorbitol; Tre: Trehalose, VP: Voges-Prausker;

Results

Fifty saliva samples (25 from COVID-recovered patients and 25 from non-COVID patients) were collected from the periodontal pocket to isolate *Streptococcus* species and tested for antibiotic sensitivity. The patients' COVID status was confirmed while obtaining the patients' consent. The patients were not segregated based on gender or age as the number of The COVID-19 recovered patients was less, and they were primarily male The isolated bacteria were differentiated based on gram staining results, hemolysis pattern, colony characteristics on blood agar, and nutrient agar. *S. sanguis* is a gram-positive coccus with alpha-hemolytic colonies.

Sugar fermentation was done to further differentiate between the *Streptococcal* species. Each species ferments different sugar. For example, *S. mutans* ferments mannitol, lactose, raffinose, sorbitol, trehalose arginine, and to voges-prausker tests, but *S. pyogenes* do not respond to mannitol, raffinose, sorbitol and to voges-prausker tests. Similarly, the sugar fermentation test results were recorded in Table 1. Further, the five isolated species were based on antigenic types confirmed through latex agglutination test. *S. pyogenes* and *S. mutans* belonged to group A, *S. sanguis* to group H, *S. mitis* and *S. salivarius* to viridans (Table 1).

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Table 2. Prevalence of identified *Streptococcus species* in the saliva samples of each group

Isolated bacteria	Covid recovered group (n=25)	Prevalence percentage	Non-covid group (n=25)	Prevalence percentage	P value
S. sanguis	2	8%	1	4%	0.230
S. mitis	4	16%	2	8%	0.080
S. mutans	25	100%	23	92%	0.003
S. salivarius	3	12%	1	4%	0.349
S. pyogenes	21	84%	19	76%	0.155

Table 3. Confirmation of *Streptococcus mutans* and *Streptococcus pyogenes* using PCR

Isolated bacteria	Covid recovered group (n-25)			Non-covid group (n=25)			P value
	Biochemical and antigenic test	PCR	Confirmation percentage	Biochemical and antigenic test	PCR	Confirmation percentage	
S. mutans	25	20	80%	23	19	82.6%	0.638
S. pyogenes	21	18	85.71%	19	17	89%	0.483

Of the 25 saliva samples collected from the COVID-recovered patient group, 25 *S. mutans* strains, 21 *S. pyogenes* strains, 4 *S. mitis*, 3 *S. salivarius* and 2 *S. sanguis* strains were identified using microbiological, biochemical, and antigenic tests. The prevalence percentage was 100% for *S. mutans*, 84% for *S. pyogenes* strains, 16% for *S. mitis*, 12% for *S. salivarius*, and 8% for *S. sanguis* strains (Table 4, Graph 1). Similarly, of the 25 saliva samples collected from the non-covid patient group, 23 *S. mutans* strains, 19 *S. pyogenes* strains, 2 *S. mitis*, 1 *S. salivarius*, and 1 *S. sanguis* strains were identified/ The prevalence percentage was 92% for *S. mutans*, 76% for *S. pyogenes* strains, 8% *S. mitis*, 4% for *S. salivarius* and *S. sanguis* strains. (Table 2, Fig. 1).

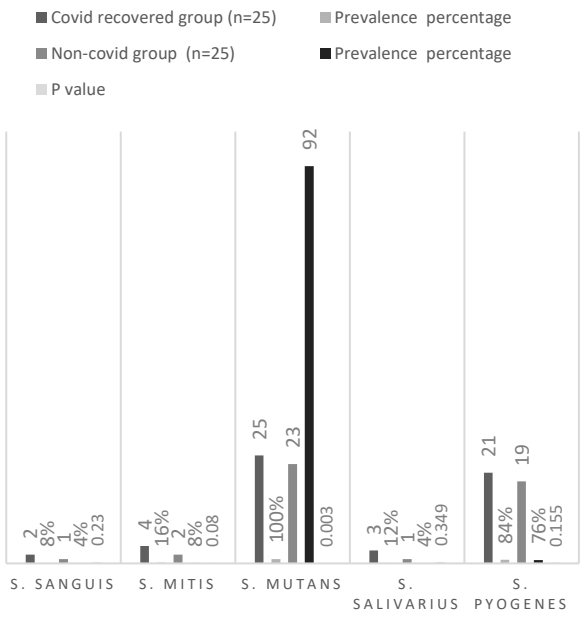

Figure 1. Prevalence of identified *Streptococcus species* in the saliva samples of each group

The species confirmation was done using PCR. Out of the 25 identified *S. mutans* strains from the samples, 20 could be confirmed using PCR. Hence, the confirmation percentage was 80%. Similarly, 18 strains out of the 21 *S. pyogenes* could be confirmed using PCR, leading to a conformation percentage of 85.71%. Following the same procedure, in the non-covid group, 19 *S. mutans* strains and 17 *S. pyogenes* strains were confirmed with PCR with a confirmation percentage of 82.6% and 89%, respectively, with a significant p-value of 0.638 and 0.438 (Table 3).

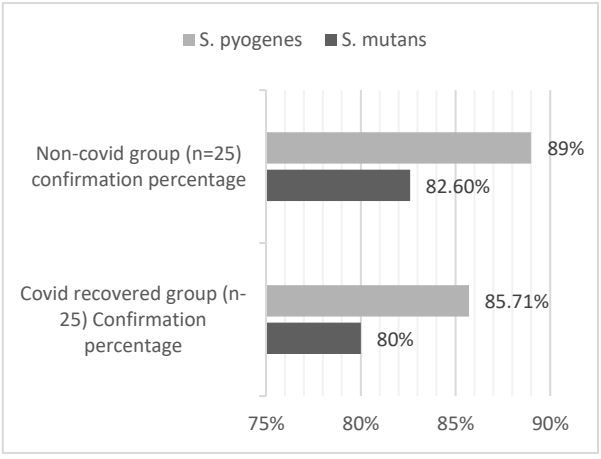

Figure 2. Confirmation of *Streptococcus mutans* and *Streptococcus pyogenes* using PCR

The isolated *Streptococcal strains* were subjected to an antibiotic sensitivity test using Kirby-Bauer's disc diffusion method. Eight antibiotics were used, which are the commonly prescribed antibiotics by dentists. The antibiotics used were Azithromycin, Clindamycin, Clarithromycin, Doxycycline, Erythromycin, Ciprofloxacin, Cefuroxime, and Amoxicillin Clavulanic acid. From the covid-recovered patient group, the *S. mutans* strains showed the maximum resistance to Azithromycin and Erythromycin, where 84% of strains were resistant, and the least resistant was towards Amoxicillin Clavulanic acid. Similarly, the *S. pyogenes* strains showed the maximum resistance to Erythromycin, where 95.23% of strains

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were resistant, and the least resistance was towards Cefuroxime with 76.19%. *S. sanguinis* and *S. mitis* recorded 100% resistance to Azithromycin and Ciprofloxacin. The resistance percentage of all the isolated strains is recorded in Table 4. Likewise, from the non-covid patient group, the *S. mutans* strains showed the maximum resistance to Doxycycline, where 65.21% of strains were resistant, and the least resistant was towards Cefuroxime. Similarly, the *S. pyogenes* strains showed the maximum resistance to Doxycycline and Erythromycin, where 63.15% of strains were resistant, and the least resistance was again towards Cefuroxime with 36.84%. *S. sanguis* and *S. mitis* recorded no resistance to most antibiotics. The resistance percentage of all the isolated strains from the non-covid group is recorded in Table 4.

Table 4. Resistance percentage of the isolated strains from the saliva samples of the covid recovered and the non-covid group toward the commonly prescribed antibiotics by dentists (in %; N=35)

Covid recovered group	Isolated bacteria	Number of isolated strains used	Resistance percentage to the commonly prescribed antibiotics by dentist (in %)							
			Az	Cd	Cth	Dx	Ery	Cpf	Cfx	Amx-Ca
	S. sanguis	2	100	50	50	50	100	100	50	50
	S. mitis	4	100	50	50	50	75	100	50	25
	S. mutans	25	84	76	68	76	84	72	80	60
	S. salivarius	3	66.6	66.6	66.6	66.6	66.6	66.6	66.6	33.3
	S. pyogenes	21	90.47	80.95	80.95	85.71	95.23	85.71	76.19	85.71
Non-Covid Group	*S. sanguis*	1	0	0	0	0	0	0	0	0
	S. mitis	2	50	50	0	100	0	0	0	0
	S. mutans	23	52.17	47.82	60.8	65.21	56.52	43.47	34.78	39.13
	S. salivarius	1	100	100	0	100	0	0	0	0
	S. pyogenes	19	57.89	47.36	52.63	63.15	63.15	57.89	36.84	42.10

Note: Az: Azithromycin; Cd: clindamycin; Cth: Clarithromycin; Dx: Doxycycline; Ery: Erythromycin; Cpf: Ciprofloxacin; Cfx: Cefuroxime; Amx-Ca: Amoxicillin Clavulanic acid

Discussion

Streptococcal infection is a common issue in almost all age groups of patients, irrespective of gender. Likewise, antibiotic resistance in *Streptococcus* has also risen in the last few decades. It is a well-known fact that the use of antibiotics leapt significantly during the COVID era. People took antibiotics irrespective of whether they were prescribed or not, which has given a significant boost to antibiotic resistance. This study primarily focused on antibiotic resistance in *Streptococcal* species affecting the oral cavity. It was discernible that the *Streptococci* strain isolated from the COVID recovered group showed more resistance to the antibiotics than those isolated from the non-covid group. In particular, *S. mutans* and *S. pyogenes* strains, the primary oral pathogenic bacteria, were resistant to most antibiotics tested in this study. Occurrences of co-infections were reported from hospitalized COVID-19 patients from UAE. Isolation and characterization of MDR strains of *Streptococcus* and *Candida* species were reported in the above study [21]. COVID-19 was linked with an increase in periodontal infections during the pandemic due to a compromised immune system, elevated levels of cytokines, DNA damage and increased virulence levels of periodontitis-causing bacteria[22]. Antibiotic overuse can select microorganisms with resistance. Antibiotics are often recommended for dental infections or prophylaxis before treatments. Failure to finish an antibiotic course may leave more resistant bacteria. These bacteria can multiply and cause drug resistance. Some oral bacteria resist antibiotic classes, making treatment more challenging [23, 24]. *S. mutans* and *Porphyromonas gingivalis*, which cause tooth cavities and periodontal disease, are multidrug-resistant. Conjugation, transformation, and transduction can provide oral bacteria resistance genes. This lets resistance characteristics spread quickly among oral bacteria species. Biofilms on tooth surfaces or oral tissues protect these bacteria from antibiotics. Biofilms allow bacteria to share genetic material and communicate, developing resistance [25].

Antibiotic resistance has been affected by the COVID-19 pandemic, but the exact type and amount of this effect may depend on several factors. Antibiotics have been used often, sometimes wrongly, to treat secondary bacterial infections in COVID-19 cases during the pandemic. There is no doubt that the COVID-19 pandemic has affected antibiotic resistance; however, the precise magnitude and type of this influence may vary based on several different conditions. The use of antibiotics to treat secondary bacterial infections in COVID-19 patients has been widespread during the pandemic, and there have been instances when they have

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been used unnecessarily [26, 27]. Moreover, antibiotics have been used as a preventative measure in certain instances, notably in patients in critical condition. Both the inappropriate use of antibiotics and their excessive usage has played a role in developing antibiotic resistance. Since the major emphasis was on COVID-19, attention and resources may have been diverted away from surveillance efforts for antibiotic resistance and antimicrobial stewardship programs. Because of this lack of monitoring and oversight, there is a possibility that incorrect antibiotic prescribing practices will rise, which will further contribute to developing bacteria resistant to antibiotics[28-30].

The pandemic's burden on healthcare systems may have contributed to challenges in providing adequate care for bacterial diseases. This strain included hospitals and clinics that were already operating at capacity. This could lead to a delay in the detection and treatment of bacterial infections, which has the potential to result in more severe cases and an increase in the usage of antibiotics. Because of the extensive usage of personal protective equipment (PPE) during the pandemic, such as masks and gloves, there is a possibility that antibiotic-resistant bacteria will be able to thrive[28-30]. The spread of microorganisms that are resistant to treatment can occur when PPE is misused, reused, or not disinfected adequately. There is a possibility that antibiotic research and development efforts have slowed considerably because of the redirection of money and attention into COVID-19 research. Therefore, the development of novel antibiotics and alternative treatments necessary to tackle illnesses resistant to antibiotics may be hampered [31, 32].

Many studies have suggested possible ways to address the above problem. They recommended a suitable antibiotic usage policy to address the above problem. Tan et al. 2023 reported the difference in oral flora and dysbiosis between COVID-19 and non-covid patients, particularly in elderly patients [33]. Also, Mihra et al., 2020 and Bessa et al., 2022 suggested using a combination of antibiotics for managing oral health and probiotics for combatting dysbiosis [34, 35]. Reports suggest using antimicrobial peptides (AMPs) for treating oral infections instead of chlorhexidine and calcium hydroxide, which dentists have traditionally used.[36] An Indian study reported using Baicalein (5,6,7-trihydroxyflavone) to control the antibiotic-resistant strains of *S. mutans,* which had high virulence and biofilm-causing capacity. Also, it was reported that it did not affect normal commensals of the oral cavity[36]. Reports suggest employing alternative methods like nanoparticles or nanotechnology to control oral infections or using herbal medicines or photodynamic therapy to reduce antibiotics[37,38]. New modified safety regulations can be implemented in dental hospitals and clinics to reduce infections. There can be increased awareness of the use of antibiotics both in dentists and patients to reduce the burden of MDR *Streptococcus* species[39].

Nanopore technology has great potential in combating MDR bacteria. This technology helps rapidly identify the bacteria and the resistant gene through rapid analysis and whole genome sequencing of the bacterial genetic material. Compared to traditional sequencing methods, nanopore sequencing can be more affordable, especially for large-scale projects. Nanopore technology can directly sequence RNA without the need for reverse transcription, preserving information about RNA modifications[40].

The data obtained can be used to design specific antimicrobial drugs to destroy MDR strains and are beneficial for rapid diagnostics and research. This technology, along with other *in silico* methods, can also be used to surveillance MDR strains and predict possible outbreaks and pandemics[41]. The portable nature of nanopore sequencers makes them suitable for use in remote settings, enabling on-site testing and monitoring of bacterial resistance patterns. The data generated can aid in the development of new antibiotics and therapies by revealing potential targets for drug design[42]. However, compared to other techniques like Illumina sequencing, nanopore sequencing has higher error rates, which might make data interpretation more difficult. Sophisticated bioinformatics techniques and significant computational resources may be needed due to the volume of data generated. Even if the technology is advancing, certain high-throughput sequencing techniques may still outperform it in terms of throughput. Long reads may be produced, although shorter reads and varying degrees of precision are also possible. The quality of the input sample might have a considerable impact on the outcomes; hence it is important to handle and prepare the sample carefully. Some laboratories may find it difficult to implement and maintain nanopore technology since it requires specific knowledge.[43] Overall, nanopore technology improves our ability to detect, monitor, and respond to MDR bacteria, potentially reducing their influence on public health; nevertheless, its limits must be carefully considered in the context of specific applications.

Conclusion

In conclusion, there has been a significant rise in the MDR strains of *Streptococcus* species in India and globally. In our study, COVID-19-recovered patients had more *Streptococcus* species isolated from their oral cavity than strains isolated from the healthy controls. Our study also concluded that the strains isolated from COVID-19 recovered patients were resistant to more antibiotics than those isolated from non-covid patients. Notably, more resistant *S. mutans* and *S. pyogenes* strains are alarming. Hence, alternative strategies have to be opted for dealing with such virulent MDR strains.

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ULTRASOUND - ASSISTED REMOVAL OF IMPALPABLE CONTRACEPTIVE IMPLANTS AT THE KORLE BU TEACHING HOSPITAL

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Abstract

Objective: To describe our experience of using ultrasonography to locate and remove impalpable implants in a low-resource environment.

Methodology: We report a series of non-palpable subdermal contraceptive implants with unsuccessful removal attempts at other facilities, who were referred to the Reproductive Health Unit, KorleBu Teaching Hospital, between 2015-2018. A high-resolution linear-array probe ultrasound was done to localize the implants. Removal was performed under local anaesthesia, involving a longitudinal incision within the ultrasound-guided skin markings and blunt dissection to locate and retrieve the implant.

Results: Fifteen patients with non-palpable subdermal contraceptive implants were referred after failed attempts by midwives or gynaecologists over the period. Implants included Implanon (9) and Jadelle (6), with durations of use ranging from 8 months to 5 years. Most implants were successfully located using high-resolution linear-array ultrasound probe, and removed under local anaesthesia. Implants were abnormally positioned in 5 cases, with depths ranging between 5 mm and 7 mm. In 14 cases, removal was successful through skin marker guidance or direct ultrasound guidance. One case required general anaesthesia and plastic surgeon's assistance. No significant complications were reported.

Conclusion: In Ghana, the increasing incidence of impalpable contraceptive implants necessitates the use of interventional radiological methods for removal. Our case series demonstrates that ultrasound-guided removal of non-palpable implants is effective and can be performed with minimal complications in low-resource settings. We recommend training providers, including midwives, in ultrasound-guided implant removal techniques and advocating for early referral to specialized centers to ensure timely and successful removal.

Key words: *contraceptive, cost-effective, difficult, implant, low-resource, non-palpable, removal, successful ultrasound scans*

Introduction

Subdermal contraceptive implants have been widely used in Ghana since the 1980s, offering high effectiveness and acceptability.[1] Studies have shown that implants like Implanon, Norplant, and Jadelle are highly effective contraceptive methods with no significant differences in effectiveness or continuation rates.[2,15]

While subdermal contraceptive implants are typically inserted subdermally in the upper arm and are designed to be easily palpable for straightforward removal. However, an increasing number of cases involve impalpable or deeply placed implants, presenting significant challenges for healthcare providers.[3] Impalpable implants can result from factors such as incorrect insertion, migration, tissue encapsulation, or significant weight gain.[3] Failed removal attempts by midwives or general practitioners may cause patient discomfort, delayed care, and potential legal issues.[3]

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To address these challenges, specialized referral clinics have been established for difficult removals.[4] Interventional radiological methods, such as high-frequency point-of-care ultrasonography, have proven effective in localizing non-palpable implants, enabling successful in-office removals in up to 96% of cases, including subfascial placements.[5] Standardized protocols now guide clinicians through safe and efficient removal procedures.[6] However, the specialized equipment required for these procedures can be costly, making reimbursement considerations essential in resource-limited settings.[5]

This study focuses on the assessment and removal of impalpable subdermal contraceptive implants using ultrasound guidance at Korle Bu Teaching Hospital. The objective is to describe the profiles of affected patients, procedural techniques, and outcomes to highlight the importance of ultrasound in managing these challenging cases.

Materials and Methods

Study design

This was a retrospective cohort study conducted by reviewing the charts of patients referred for the assessment and removal of non-palpable subdermal contraceptive implants.

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Study Site

The study took place at the Family Planning & Reproductive Health Unit of Korle Bu Teaching Hospital, Ghana, between January 2015 and August 2018.

Selection Criteria

Patients were eligible for inclusion if they met the following criteria: (1) documented insertion of a subdermal contraceptive implant (Implanon or Jadelle) based on medical records, (2) non-palpable implant on physical examination, and or (3) a history of failed removal attempt by trained midwives or obstetrician-gynaecologists.

Data Capture and Analysis

Patient demographics, implant characteristics, ultrasound findings, procedural details, and outcomes were collected and analyzed. Descriptive statistics were used to summarize the data.

Procedures

History and Examination

An experienced provider evaluated all patients at the outset. A detailed history was taken to confirm that the implant was actually inserted, the type of implant, the duration of the patient's use of the implant, and the reasons for its removal (Table 1). A physical examination of the implant insertion site was performed once more to establish that the implant was in fact "impalpable." When properly inserted, the proximal end of the rod should be approximately 1 cm away from the scar at the insertion site. An ultrasound examination was then scheduled and performed by a skilled reproductive health specialist.

Implant Identification

A high-resolution linear array ultrasound probe (7–10 MHz, Philips Clearvue 350) was used to localise the implant. The scan was performed with the patients in the operational position (supine, shoulder abducted to 90° in external rotation, elbow in 90° flexion, and the patient's hand behind her head). This is the same operative position that is required for removal.

A systematic ultrasound-guided search was conducted in the transverse plane (perpendicular to the humeral length surrounding the insertion scar) and then rotated to the longitudinal plane. The implant was identified in the transverse plane by the rod's characteristic posterior acoustic shadowing, which appeared as a thin, dark wedge reaching deep to the rod. The implant was demonstrated as a bright echogenic 'dot' at the peak of the acoustic shadow (Figure 1). The probe was guided proximally and distally along the trace of the echogenic dot and shadow to confirm that the identified structure fits the implant's expected dimensions. Once detected, the ultrasound probe was rotated through approximately 90º to be in a parallel line with the implant. The bright reflection of the implant could then be appreciated (Figure 1).

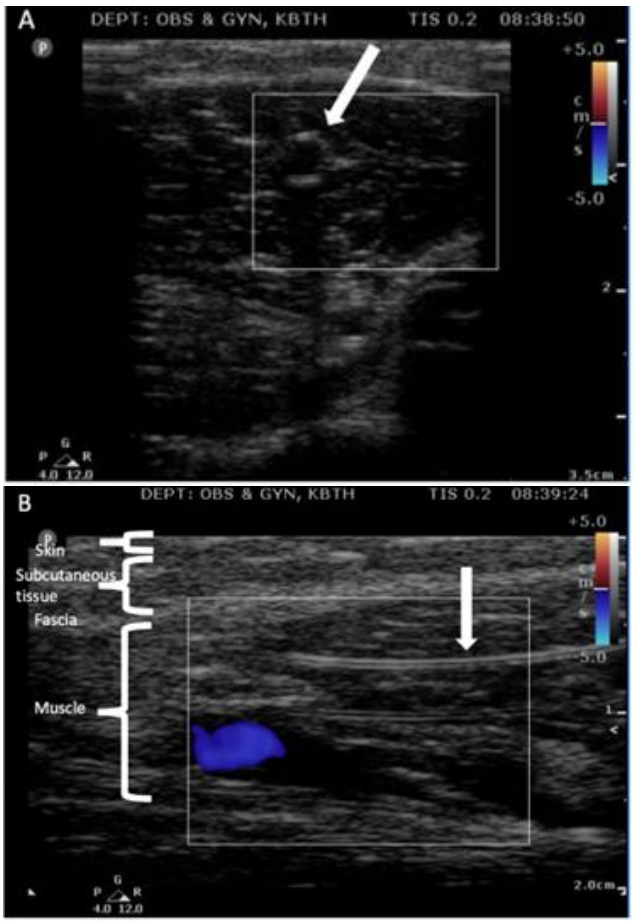

Figure 1: An ultrasound image of contraceptive implant in upper arm

A- Transverse plane with the echogenic dot of the contraceptive implant seen with a posterior acoustic shadow

B- Probe rotated through approximately 90º to be in a parallel line with the implant.

Figure 2: Ultrasound directed skin marking of contraceptive implant with black permanent marker before removal.

--➔ Scar from original insertion point

⟶ Arrow indicates scars from previous failed attempts also seen on the arm.

The skin area was marked with a permanent marker pen once the implant's anatomical site was determined (Figure 2). While marking, the operator made certain that the implant's shadow remained in the centre of the US screen. This outlined mark denoted the whole length of the implant in order to facilitate removal. The scanning probe was gently pressed against the arm, while preventing compression, in order to reduce skin-implant depth measuring errors. Following the ultrasound guided marking, an implant removal procedure was organised in the day surgical unit.

Implant Removal

The steps involved careful cleaning of the skin and draping of the arm using aseptic procedures during the implant removal. The provider injected 2 ml of a 1 percent Lidocaine local anaesthetic preparation beneath, rather than above, the evaluated depth of the marked implant rod. This prevented the skin-implant depth from increasing. Within the ultrasound skin markings, a longitudinal incision (1.5 to 2 cm) was created, followed by blunt dissection until the implant was first palpated through the incision by the provider's finger. The dissection was continued bluntly until the implant was visually spotted and retrieved with small curved artery forceps. Subcutaneous absorbable sutures and subcuticular suturing were used to close the wounds. During this series, the average removal time was about 10 minutes. Following that, patients were given wound care instructions, counselled on contraception while the implant was removed, and discharged home the same day with advice to use barrier methods (which were given them) until they were decided on other long-term methods. Three days after discharge, follow-up visits were scheduled, and advice was given to attend the community clinic for future follow-up.

All 15 individuals in our cohort had their subdermal contraceptive implant successfully removed. With the exception of one case that required sedation and the assistance of plastic surgeons, all removals were completed on the first attempt, with no significant complications following the procedure or at the follow-up visit.

Results

A total of 15 patients with non-palpable subdermal contraceptive implants were referred to the Family Planning & Reproductive Health Unit at Korle Bu Teaching Hospital for ultrasound-guided removal. The implants included Implanon (9 cases) and Jadelle (6 cases), with durations of use ranging from 8 months to 5 years (Table 1). All patients had previously undergone unsuccessful removal attempts by trained midwives or obstetrician-gynaecologists from various healthcare facilities in Ghana.

Ultrasound successfully located the implants in all 15 cases. The depth of the implants ranged from 5 mm to 7 mm beneath the skin surface. The implants were classified as normally positioned in 10 cases and abnormally positioned in 5 cases. Despite these challenges, all implants were successfully removed. Fourteen removals were completed on the first attempt using skin marker guidance, with some cases facilitated by direct ultrasound visualization. One case (Client I) required sedation and assistance from plastic surgeons due to the deeper placement (7 mm).

Majority of skin-marking guided impalpable implants were removed under local anaesthesia, with only one case requiring sedation and assistance from plastic surgeons before removal could be achieved. At the point of removal, some cases were facilitated by direct visualisation with ultrasound guidance.

The procedure was performed under local anesthesia in all but one case, and no significant complications occurred during or after the procedures. Patients were discharged the same day and attended follow-up visits, where no adverse outcomes were noted.

Discussion

Principal Findings

We reported a series of 15 cases of non-palpable contraceptive implants successfully removed using ultrasound guidance in Ghana. The use of ultrasound guidance in the removal of non-palpable subdermal contraceptive implants was found to be a safe and effective method. All 15 patients in the study had their implants successfully removed with no significant complications, except for one case that required sedation and assistance from plastic surgeons. With this particular case, the implant had migrated into the axilla. This case series highlights the potential benefits of using ultrasound guidance in low-resource environments where trained midwives or obstetrician specialists may not be available to perform the procedure and also where

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MRI services may be expensive and not be widely available.

Results

Similar findings have been reported in other studies conducted in high-income countries such as the United Kingdom[7] and the United States[8] which also demonstrated the effectiveness of ultrasound guidance in locating and removing impalpable implants. In addition, reports from Nigeria and the Unitd States of America also reported successful removal of subdermal contraceptive implants using ultrasound guidance.[8,9] Ultrasound guidance has been shown to improve the success rate of implant removal, particularly in cases where the implant is difficult to locate or has migrated from its original insertion site.[7] This is in contrast to blind removal techniques, which may result in incomplete removal or traumatic injury to surrounding tissue.

Clinical Implications

The use of ultrasound guidance can help to minimize complications such as bleeding or infection, as the procedure can be performed with greater accuracy and precision.[8] There were no such complications among any of our clients. However, the use of ultrasonography requires specialist radiologists and a high-frequency linear probe to ensure proper location of the implant.[10,11] It is also important to note that failure to detect an implant by ultrasound may be due to several factors, including a low frequency ultrasound probe, obesity, or limited experience of the sonographer in dealing with a subdermal implant scan.[10,11,17] Our work used a high-resolution linear array ultrasound scan by an experienced specialist.

It is worth noting that inadequate training and lack of experience in implant insertion have been linked with poor implant placement and impalpable implants.[16] Proper training and continuing education for healthcare professionals who insert implants can help to reduce the occurrence of impalpable implants.[12] In addition, it is crucial to conduct routine follow-up visits after insertion to assess the implant's position, palpability, and any adverse effects.

Policy Implications

The introduction of Nexplanon into Ghana in 2015 was a significant step towards improving access to long-acting reversible contraceptives (LARCs) for women. The Ghana Health Service - Family Health Division, and other partners, provided training and orientation for service providers to ensure safe and effective implant insertions.[13] However, the discontinuation of Implanon Classic production in favour of Implanon-NXT manufacture, which led to the introduction of Nexplanon, has not entirely eliminated the use of other subdermal implants such as Jadelle and Sinoimplant II, and Implanon, which are still used by some women.[14] As a result, removing impalpable subdermal implants may continue to be a challenge in the future. This highlights the importance of ensuring that service providers are adequately trained and skilled in the insertion and removal techniques of all types of subdermal implants, not just Nexplanon. It is essential to have a comprehensive and ongoing training program for all providers to ensure that they are up to date with the latest techniques and procedures for inserting and removing subdermal implants. Furthermore, increasing awareness among women about the potential complications associated with subdermal implants, including impalpable implants, is crucial. Women should be informed about the importance of regular self-examination and seeking medical attention if they cannot feel the implant. This will ensure timely intervention and prevent the development of complications such as migration, fibrous adhesion, and nerve or blood vessel damage.

Research Implications

This work retrospectively reports a case series to document the effectiveness of ultrasound scan as a useful intervention in managing non-palpable implant removals. A more rigorously designed prospective study including randomized control trials are needed to critically evaluate this intervention and compare with others.

Strengths and Limitations

This case series highlights the potential benefits of using the technology of ultrasound guidance in low-resource environments where the numbers of trained midwives or gynecologists are grossly inadequate, to perform the procedure and also where MRI services may be expensive, unaffordable and not be widely available. A major weakness in this work is the inherent limitations of case series that lack prospective recruitment and randomization to eliminate selection bias among others.

Conclusion

Impalpable subdermal contraceptive implants pose a significant challenge in their removal, especially in low-resource settings. Ultrasonography can be an effective and low-cost tool for locating and removing impalpable implants. Proper training and continued education of contraceptive service providers in implant insertion techniques can help to reduce the incidence of impalpable implants. Further studies are needed to evaluate the effectiveness and safety of this method in larger populations.

Author Contribution

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DETERMINATION OF SALIVARY LACTOFERRIN LEVELS BEFORE AND AFTER NON-SURGICAL PERIODONTAL TREATMENT IN PATIENTS WITH AGGRESSIVE PERIODONTITIS

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Abstract

Objective: This study determined levels of Salivary lactoferrin (sLf) before and after non-surgical periodontal treatment (NSPT) in individuals with localized and generalized aggressive periodontitis compared to healthy controls.

Methodology: The study was an interventional and prospective design. Nineteen participants were clinically and radiographically diagnosed as having AP and 18 participants who did not show evidence of the disease or other diseases, served as controls. All participants received NSPT which included scaling and polishing for the controls and scaling and root planing (SRP) for the cases. Unstimulated whole saliva was collected from participants before and after NSPT. Salivary Lactoferrin levels were quantified using the Human Lactoferrin ELISA kit.

Results: The mean ages were: GAP=33.80±8.93, LAP=32.11±8.07 and Controls = 31.39±8.98 years. Concentration of sLf before NSPT among the cases was 70.92±26.84 (-µg/ml-) and the controls had 48.39±28.56 (-µg/ml-). After treatment, concentration of sLf was 68.57±25.34 (-µg/ml-) for cases and 43.42±21.54(-µg/ml-) for controls. A significant difference was observed at baseline between cases and controls (p= 0.018) and after treatment (p=0.003) which indicated sLf levels were higher in the diseased than non-diseased individuals.

Conclusion: Elevated sLf levels serve as an indication for increased degree of inflammation and this biomarker can be used to determine the severity of AP.

Key words: *Saliva, Proteomic biomarker, Salivary lactoferrin, Localized Aggressive Periodontitis, Generalized Aggressive Periodontitis.*

Introduction

Aggressive periodontitis (AP) just as its name suggests, is an inflammatory disease of the periodontium, characterized by rapid attachment loss (AL) of the periodontal tissues as well as alveolar bone destruction in otherwise systemically healthy individuals.[1] There are two clinical varieties of AP: the Localized Aggressive Periodontitis (LAP) and the Generalized Aggressive Periodontitis (GAP) forms.

LAP frequently has an age onset at about puberty and is clinically characterized by interproximal tissue AL on at least two permanent teeth, one of which is a first molar, and involving no more than two teeth other than the first molars and incisors".[2,3] GAP usually affects individuals under age 30, but older patients may be affected.[2] Clinically, GAP is characterized by "generalized interproximal tissue AL affecting at least three permanent teeth other than first molars and incisors."[2] The bacteria *Aggregatibacter actinomycetemcomitans and Porphyromonas gingivalis* have been associated with LAP and GAP in mostly teenagers and young African adults.[3,4]

Arowojolu and Nwokorie[5] and Harley and Floyd [6] recorded the prevalence of AP in Ibadan and Lagos among Nigerian teenagers and young adults to be 0.8-1.6% and 0.8% respectively. In the United States, a national survey of adolescents aged 14 to 17 years reported that 0.53% had LAP [7] and 0.13% had GAP.[7] In addition, blacks were at much higher risk than whites for all forms of AP, and male teenagers were more likely to have GAP than female adolescents. Salivary Lactoferrin levels are raised in patients with periodontitis and AP not being an exception.[8]

Saliva is secreted mainly by three pairs of major salivary glands (parotid, submandibular and sublingual) and numerous minor salivary glands (450-750). [9] Human saliva is a plasma ultra-filtrate and contains proteins either synthesized in situ in the salivary glands or derived from blood and contains biomarkers derived from serum, gingival crevicular fluid, and mucosal transudate. [11]Lactoferrin is a biomarker secreted in saliva and can be used to monitor the levels of hormones, drugs and medications, bone turnover, biologic markers, forensic evidence and oral diseases which include caries and periodontal disease.[10]

The use of proteomic biomarkers such as sLF have been found to have favorable diagnostic value in addition to genomic and microbiological markers.[10] We

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hypothesized that sLf levels will be higher at baseline in patients with AP and reduced after non-surgical periodontal treatment (NSPT). The aim of this study was to determine the levels of sLf before and after NSPT in individuals with AP and control participants.

Materials and Methods

The study was an interventional and prospective design. Ethical approval for the study was obtained from the Ethical and Protocol Review Committee of the College of Health Sciences, University of Ghana (CHS-Et/M.8-P 4.6/ 2015-2016). Respondents aged 20-50 years who met the inclusion criteria according to Armitage[1] were selected for this study. Participants who had comorbid conditions, those on antibiotics and medications for systemic diseases, known alcoholics, smokers, pregnant or lactating women, and individuals who had had scaling and root planing (SRP) in the past six months were excluded.

The sample size was estimated based on effect size in terms of standard deviation of the sample differences of 0.76 as reported in a similar study by Pagano and Ganvreau.[12] Using the equation for comparisons of two means, a total of 37 individuals were estimated made up of 19 cases and 18 controls. Thirty-seven individuals who consented and met the inclusion criteria were recruited. The participants were selected consecutively from May 2016- May 2017 at the Oral Diagnosis unit of the Dental Clinic of the then UGSMD. Nineteen participants were clinically and radiographically diagnosed as having AP and 18 participants who did not show evidence of the disease or other diseases, served as controls. The controls were patients attending the dental clinic for routine dental care who did not show evidence of periodontal disease or other systemic diseases per the inclusion and exclusion criteria and after obtaining informed consent. The sociodemographic data of all the participants was captured using a structured questionnaire

Clinical Visits and Treatment of Cases and Controls

The cases had four clinical visits whiles the controls had three over a period of four weeks. At the first visit, a comprehensive periodontal examination was done and an OPG of each participant was taken. The clinical examination of all the controls and AP individuals was carried out using a periodontal chart and a form for saliva collection which had the participants initials and identification number, the tube weight before and after saliva collection, the volume of saliva collected and the duration of the collection. Protocols and guidelines for saliva collection by Wang et al.[9] was explained to the participants. At the second visit, unstimulated whole saliva was expectorated into falcon tubes provided every minute under ice in a mug over a period of 15 min. At least 3-5 ml of saliva was collected for each participant. In the dental clinic, the samples were stored in an ice chest with ice packs for 15-30 min. They were then transported to the Chest clinic laboratory for centrifugation and subsequently stored at -80ºC at the Pathology Department at Korle-Bu. All the samples were kept at the Korle-Bu Teaching Hospital and later sent to Noguchi Memorial Institute for Medical Research, Legon for laboratory analysis.

A full mouth scaling and polishing for controls which is done routinely for patients who come for regular dental visits and SRP for the cases (individuals with disease) was carried out. For the cases, 10ml of 0.2% Chlorhexidine gluconate mouthwash was used to irrigate all probing pocket depths (PPD'S) ≥ 4 mm and the solution gargled for one minute and expectorated. Oral hygiene instructions were given, and the controls seen at four weeks (third visit) after which the saliva samples were collected again using the same protocols and the comprehensive periodontal examination repeated. The cases were seen within 24 h for the second session of SRP (third visit) and then at four weeks for re-evaluation (fourth visit). Saliva samples were collected again at this time using the same protocols and a comprehensive periodontal examination done.

The samples were transferred into a centrifuge (Eppendorf 5810 R) and run at 1,071xg for 25 min at 4°C to remove insoluble materials, cell debris and food remnants. The supernatants were carefully decanted into four cryo tubes and the pellets placed into one tube. Pierce protease inhibitor cocktail EDTA-Free (5µl) was added to the supernatants and mixed. The treated samples were then transferred and stored in a −80°C freezer awaiting laboratory analysis.

Salivary Lactoferrin (sLf) measurement by ELISA

The laboratory work for sLf determination was done at the Noguchi Memorial Institute for Medical Research (NMIMR) of the College of Health Sciences, University of Ghana, Legon. Salivary Lactoferrin was quantified using the Human Lactoferrin ELISA kit (ab108882- Lot: GR232543-29 Lactoferrin (HLF2) based on the manufacturer's instructions. Saliva samples and lactoferrin standards were added to the plate in duplicate. For colour development, 50 µl/well of chromogen ($3,3^1,5,5^1$-tetramethylbenzidine (TMB) was added with the samples turning blue after the plate was incubated in the dark for 15 min. The colour reaction was subsequently stopped by the addition of 50 µl/well of stop solution (0.2 N H_2SO_4) with the colour of samples turning yellow. The samples were transferred to an ELISA plate reader (BioTek, VT, USA) and optical density (OD) read at 450 nm. Optical density data was converted to lactoferrin concentration using a 4-parameter logistic curve fit.

Data Analysis

Data was analysed using Statistical Package of Social Sciences (SPSS version 22). Chi-square test was used to compare proportions of socio-demographic data. Mean lactoferrin levels were compared using T- test for two means and ANOVA for more than two means between cases and controls. The data was presented as mean±SD. Significance level was set at $p < 0.05$.

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Results

Background Characteristics and Sociodemographic Data

The age range of respondents who voluntarily participated in the research work were from 20-50 years. The mean age and distribution of respondents with GAP, LAP and the controls can be found in Table 1. Data pertaining to the tribe, religion and educational background details of the participants were collected (Table 1).

Table 1: Sociodemographic characteristics of all respondents

	Participant category				
Demographics	**GAP n (%)**	**LAP n (%)**	**Controls n (%)**	**Total N (%)**	**P-Value**
Mean age ± Mean SD (yrs)	10(33.80 ± 8.93)	9(32.11 ± 8.07)	18(31.39± 8.96)	37(32.22 ± 8.56)	0.78
Gender					
Male	4(40.0)	6(60.0)	10(55.6)	20(54.0)	0.06
Female	6 (60.0)	3(40.0)	8(44.4)	17(46.0)	
Total	10 (100.00)	9(100.00)	18(100.00)	37(100.00)	
Marital Status					
Never Married	6(60.0)	7(77.8)	12(66.7)	25(67.6)	0.84
Married	3(30.0)	2(22.2)	3(16.7)	8(21.6)	
Divorced	1(10.0)	0(0.0)	2(11.0)	33(8.1)	
Separated	0(0.0)	0(0.0)	1(5.6)	1(2.7)	
Widowed	0(0.0)	0(0.0)	0(0.0)	0(0.0)	
Total	10(100.00)	9(100.00)	18(100.00)	37(100.00)	
Tribe					
Ga/Dangme	3(30.0)	1(11.1)	3(16.7)	7(18.9)	0.57
Akan	5(50.0)	4(44.4)	12(66.7)	21(56.8)	
Ewe	1(10.0)	3(33.3)	2(11.0)	6(16.2)	
Northern	1(10.0)	1(11.1)	0(0.0)	2(5.4)	
Other	0(0.0)	0(0.0)	1(5.6)	1(2.7)	
Total	10(100.00)	9(100.00)	18(100.00)	37(100.00)	
Religion					
Christian	10(100)	8(88.9)	18(100.00)	36(97.3)	
Islam	0(0.0)	1(11.1)	0(0.0)	1(2.7)	0.20
Traditional	0(0.0)	0(0.0)	0(0.0)	0(0.0)	
Total	10(100.00)	9(100.00)	18(100.00)	37(100.00)	
Educational background					
No Formal Education	0(0.0)	0(0.0)	1(5.6)	1(2.7)	0.25
Completed only Primary education	2(20.0)	0(0.0)	1(5.6)	3(8.1)	
Completed only Secondary education	7(70.0)	5(55.6)	7(38.8)	19(51.4)	
Completed Tertiary education	1(10.0)	4(44.4)	9(50.0)	14(37.8)	
Total	10(100.00)	9(100.00)	18(100.00)	37(100.00)	

F-test did not show any significant difference in the mean ages of the three participant groups.
Chi-square test showed no significant associations between the sociodemographic characteristics and the participant categories.

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Concentration of Salivary Lactoferrin (sLf) Measured for the Participants

The mean concentration of sLf measured before and after treatment for the cases and controls can be found in Table 2 and the details of the subgroup analysis for the cases (LAP and GAP) before and after treatment are captured in Table 3.

Table 2: Concentration of sLf levels before and after treatment for the cases and controls

	Mean Concentrations of sLf		P-value
Participant category	**sLf conc(µg/ml) Before treatment**	**sLf conc (µg/ml) After treatment**	
Cases (n=19)	70.92 ± 26.84	68.57 ± 25.34	0.44
Controls (n=18)	48.39 ± 28.56	43.42 ± 21.54	0.37
Total (n=37)	59.96 ±29.59	56.33 ±26.51	
P-value	0.018	0.003	

T- test showed significant differences in sLf between cases and controls before treatment (p= 0.018) and after treatment (p= 0.003).

Table 3: Concentration of sLf levels before and after treatment for the LAP and GAP cases

	Mean Concentrations of sLf		P-value
Participant category	**sLf conc (µg/ml) Before treatment**	**sLf conc (µg/ml) After treatment**	
LAP (n=9)	70.08 ± 26.12	74.40 ± 15.42	**0.53**
GAP (n=10)	76.94 ± 20.12	63.84 ± 31.81	
Total (n=19)	73.69 ± 22.76	68.84 ± 25.32	
P-value	**0.84**		

Repeated measure F- test showed no significant difference in the sLf concentration of the LAP and GAP groups before and after treatment (P value= 0.53 and 0.84).

Discussion

This study was conducted primarily to determine the levels of sLf and to find out if there was any association between sLf levels in participants with AP at baseline and after NSPT. Our literature search did not reveal work on this subject in sub-Saharan African populations. The present study was therefore regarded as part of an early effort to determine whether a link exists between AP and the concentration of sLf among sub-Saharan African populations.

There were 20 males and 17 females who participated in the study. Among the cases, 10 (54.0%) and 9 (46.0%) of the males and females respectively had AP (Table 1). Among the cases, 4 (40%) males and 6 (60.0%) females had GAP whilst 6 (66.7%) males and 3 (33.3%) females had LAP (Table 1). Comparing our results to a study by Fine et al.,[13] 10 patients with LAP and equal number of controls were matched for age, gender and race. The African Americans were 7 in each group whiles the Caucasians were three 3 in each group. In yet another study by Suomalainen et al.,[14] 7 participants with LAP and the same number of controls were recruited in Finland. This reveals the low numbers of Caucasians with the disease.

The mean age in this study for GAP (33.8 ± 8.93) years, LAP (32.11± 8.07) years and control (31.39 ± 8.96) years respondents was slightly higher compared to the mean age of the respondents in a study by Fine et al.,[13] which recorded the mean age of participants with LAP to be 18.9 ± 7.0 years and that for the controls to be 19.7±7.4 years. In another study by Rocha et al.,[15] on 'Differential expression of salivary glycoproteins in aggressive and chronic periodontitis,' the average age for AP participants was 19-28 years which was close to the age range captured in our study.

The normal lactoferrin concentration in saliva is 8µg/ml. [8] Among salivary proteins, sLf is the most important factor of natural immunity. Its concentration corresponds to 8.96 and 7.11 µg/ml in unstimulated and stimulated saliva, respectively.[8] Our literature search did not reveal baseline levels of lactoferrin in saliva of individuals with AP.

The sLf concentration in the oral cavity is related to different fluid samples to be assayed (whether stimulated or unstimulated saliva or gingival crevicular fluid)[8]. The results of the concentration of sLf in this present study compares with those of other published work even though differences existed in the samples collected, methods and participants used.[15,16,17] In this present study, the concentration of lactoferrin was quantified using ELISA. The concentration of lactoferrin obtained at baseline and also comparing before and after NSPT using whole unstimulated saliva were consistent with the views expressed by other investigators even though some studies focused on the iron content of sLf, use of stimulated saliva, gingival crevicular fluid and serum.[8,15,16,17]

Unique to this work was the introduction of GAP cases which most studies in the literature did not report on (Table 3). Re-evaluation after initial periodontal therapy in one month was considered in this study which was not indicated in some of the reports read.

In this study, the results obtained at baseline and after treatment between the cases and controls were significant (P = 0.018) and (P = 0.003) respectively (Table 2). The observed drop in lactoferrin concentration among the cases after treatment was not significant. It did not approach the levels of the healthy controls. The differences in sLf before and after the

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NSPT for both the GAP and LAP cases were not significant. A study by Berlutti et al. [19] confirmed an increase in lactoferrin levels from 20 to 60 μg/ml during infection and inflammatory processes and this was attributed to the recruitment of neutrophils which increases sLf concentration. It was also reported by Malathi et al. [20] that, during gingival inflammation, lactoferrin was strongly upregulated and detected at a higher concentration in saliva of patients with periodontal diseases as compared to healthy patients. The reduction in the levels of lactoferrin as recorded in the literature can reach normal levels in a non-inflammatory state.[18]

Furthermore, lactoferrin was found to be strongly up-regulated in mucosal secretions during gingival inflammation and detected at high concentrations in saliva of patients with periodontal disease compared with healthy patients in a study by Giannobile et al.[21] An elevated level of lactoferrin was also observed in the saliva of participants with periodontitis in a study by Kumar et al. [22] and their levels decreased following NSPT. In this study, the respondents were re-evaluated at four weeks and a decrease in sLf levels were detected between the cases and controls. These findings are in agreement with another study by Buchmann et al.[23] who concluded that clinical healing in chronic periodontal disease is associated with a down regulation of local polymorphonuclear responses following NSPT.

In a review by Narang et al. [24] on 'Salivary Biomarkers for Periodontal Diseases', it was reported that the biomarkers during gingival inflammation were detected at high concentrations in saliva of patients with periodontal disease compared with healthy patients. These results were consistent with the current findings with regards to the cases and controls. The overall increase and decrease in sLf concentration obtained in this study among AP participants before and after NSPT respectively are consistent with some studies with designated increased levels of this biomarker when compared to control participants without periodontal disease.

The results of the study did not support our hypothesis probably due to the low sample size and re-evaluation period, but a significant difference was observed between cases and controls at baseline (p= 0.018) and after treatment (p=0.003) which indicated sLf levels are higher in the diseased state than the non-diseased state. The elevated sLf levels serve as an indication for increased degree of inflammation and this is a biomarker to determine the severity of the periodontal disease. After treatment, this can be measured to indicate possible effective treatment outcomes.

Conclusion

At baseline, sLf levels were significantly different from the cases and controls. The significant difference persisted even after treatment. There were no significant changes in sLf levels for both cases and controls after treatment. This study demonstrated that, sLf levels change with the LAP and GAP conditions.

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Declaration

Part of the original data has also been published in an earlier article under a different title with a different outcome as, "*Total Salivary Immunoglobulin A Determination Before and After Non-Surgical Periodontal Treatment in Patients with Aggressive Periodontitis*". (J Surg Res 2022; 5 (2): 322-331)".

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A COMPARATIVE SCANNING ELECTRON MICROSCOPIC STUDY OF THE EFFICACY OF THREE GUTTA-PERCHA SOLVENTS USED DURING ENDODONTIC RETREATMENT

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Abstract

Objective: This study sought to compare the number of unfilled dentinal tubules in the root canals using a Scanning Electron Microscope (SEM) after the use of K-files and the respective solvents (Chloroform, Eucalyptol, D-limonene).

Methodology: The study was a prospective comparative study. Single-rooted teeth extracted because of various dental conditions were root-treated using the rotary ProTaper system and stored in normal saline. After three months, the teeth were randomly assigned to the three solvent groups (Chloroform, Eucalyptol, and D-limonene). Gutta-percha was removed using the solvent and K-files. The teeth were then divided longitudinally and the root canal surfaces (apical third, middle third, and coronal third) were examined using a scanning electron microscope to determine the number of unfilled dentinal tubule orifices per unit area.

Results: D-limonene had the greatest number of unfilled dentinal tubules across the three segments of the divided teeth while Chloroform had the least number of unfilled dentinal tubules

Conclusion: D-limonene had superior gutta-percha removal abilities as compared to Eucalyptol and Chloroform.

Key words: *Endodontic Retreatment, Chloroform, Eucalyptol, D-limonene, SEM*

Introduction

Endodontic retreatment is a procedure performed on a previously root-treated tooth which requires additional new endodontic treatment to achieve a successful outcome.[1,2] Its main objective is to remove all the obturation material from the root canal system and to regain access to the apical third of the root canal system.[3] Remnants of the previous obturation material may harbour microorganisms, cause their growth and multiplication and subsequently lead to failure of the retreatment.[4,5] The clinical success rate of endodontic retreatment has been estimated to vary between 50% and 90%.[6] Endodontic retreatment is indicated in any of the following scenarios: when clinical symptoms are present, when radiographic signs of failure are shown, when elective root canal treatment is indicated, and when endodontic treatment is incomplete even if clinical or radiographic signs are not present.[3]

Gutta-percha (GP) has been the most used root canal obturation material for more than a century.[7,8] In Ghana 98.4% of dentists studied, used gutta-percha as a root canal obturation material.[9]

Several techniques can be employed to remove gutta-percha from the root canals during endodontic retreatment. e.g. the use of heated instruments, mechanical e.g. rotary and hand files, ultrasonic tips and files, chemical e.g. solvents, lasers or a combination of any of these.[3,8,10] Regardless of the GP removal technique used, studies have shown that the root canal dentine walls are never completely free of GP.[11,12,13]

In a study by Ampofo et al. in Ghana[9], 61.3% of respondents reported using hand files in combination with solvents and Gates-Glidden burs to remove gutta-percha during re-endodontic treatment. Chloroform, Eucalyptol, and Orange oil (D-limonene) were found to be the three most commonly used solvents by Ghanaian dentists[9].

Dental gutta-percha is composed of 18.9% to 21.8% gutta-percha, 59.1% to 75.3% zinc oxide filler material, 1.5% to 17.3% metal sulphates which confer radio-opacity, and 1.0% to 4.1% wax and/or resin which act as plasticizers.[14,15,16] Gutta-percha is a non-polar material. Effective gutta-percha solvents are weakly polar or non-polar. These solvent molecules can effectively penetrate the gutta-percha polymer strand and cause their separation and subsequent softening or dissolution.[17] Chloroform is a polar solvent but has weakly non-polar properties. Both D-limonene and Eucalyptol are non-polar solvents.[18] When solvents are applied to a polymer, the polymer absorbs the solvent and swells. The swelling softens the polymer and when more solvent is added, dissolution begins.[19]

Chloroform and Eucalyptol are the most widely used solvents by dentists worldwide but they have some undesirable properties. Chloroform has been categorized as a 2B carcinogen by the International

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Agency for Research of Cancer.[20] Eucalyptol has a pungent odour which is discomforting to some patients and needs to be heated before it can soften gutta-percha maximally.[21] These undesirable properties have led many dentists to turn to alternative gutta-percha solvents from the essential oil family. D-limonene is refined orange oil.[22] It is safe, biocompatible, has low cytotoxicity, and is non-carcinogenic.[22] In dentistry, it has been used for the dissolution of zinc oxide cemented root fillings.[7,22]

This study sought to compare the number of unfilled dentinal tubules in the root canals using a Scanning Electron Microscope (SEM) after the use of K-files and the respective solvents (Chloroform, Eucalyptol, D-limonene).

Materials and Methods

This was a prospective comparative study which was performed on 42 extracted maxillary single-rooted whole human teeth which had been extracted because of poor periodontal support.

The clinical component of the study was carried out in the Clinical Simulation Laboratory (Phantom Head Clinic) of the Restorative Department of the University of Ghana Dental School (UGDS), Accra. The Scanning Electron Microscope evaluation and analysis was carried out at the Environmental and Safety Engineering Department of the University of Mines and Technology (UMaT), Tarkwa.

Adult maxillary central and lateral incisors with lengths between 19mm to 25mm were included in the study. Teeth with the following characteristics were excluded from the study: root or crown fractures, the presence of internal or external resorption, caries, root canal or pulp chamber calcifications, dilaceration of roots, open apices, previously root-treated teeth, and cervical tooth surface loss that involved the pulp.

The teeth used in the study were obtained from the Tooth Bank of the Oral Diagnosis and Maxillofacial clinics of the University of Ghana Dental School, Korle-Bu. A total of 42 whole teeth comprising 24 central incisors and 18 lateral incisor teeth were selected. The teeth were transferred into a storage container containing 10% formalin. Soft tissue and calculus were manually removed from the tooth surfaces with a universal scaler.

A periapical x-ray machine (Carestream CS2 100, Japan) was used to take digital periapical x-rays using the paralleling technique to confirm the patency of the canals and also to confirm the absence of internal resorption.

The cleaned teeth were subsequently embedded in wax moulds that contained a mixture of dental plaster and sawdust to enable easy handling of the teeth during the root canal procedure.

Endodontic treatment was carried out using the DTE Endo Radar Plus Endodontic Motor (Guilin Woodpecker Medical Instrument Company Limited, China) and ProTaper Universal Files (Dentsply Maillefer, Switzerland) and using the ProTaper crown down filing technique.

Irrigation was done with 2.5% sodium hypochlorite (Milton, Procter and Gamble, United Kingdom) using a size 27-gauge side-vented needle (Eoskyo, Guangzhou, China).

Finishing file F1 was used to complete the shaping and cleaning of the lateral incisor canals and Finishing files F1 and F2 were used for the central incisor canals. 17% ethylenediamine tetraacetic acid (EDTA), (Prevest DenPro Limited, India) was used to lubricate the canals during filing.

A final irrigation of the canal was done with 2.5% sodium hypochlorite. The canals were dried with paper points (Technical &General Ltd, London, England) and master cones corresponding to the finishing files were lightly coated with Sealapex (Kerr, Italy) and positioned into the canal.

Excess gutta-percha was removed with the use of a heated instrument. The access cavities were restored with Glass Ionomer Cement (Prevest DenPro Limited, India). The teeth were taken out of the moulds with the sawdust and plaster fillings and cleaned.

Post-obturation x-rays were then taken to confirm the canal spaces were well-obturated and without voids. The root-treated teeth were kept in normal saline at room temperature for three months to simulate intraoral conditions.

After three months, the teeth were separated into two groups; maxillary central incisors and maxillary lateral incisors. A simple randomisation technique was used to allocate the root-treated teeth into the three solvent groups i.e., Chloroform (VWR Chemicals BDH, France), Eucalyptol (Silver Bird Eucalyptus oil, Bells, Sons & Co. United Kingdom), and D-limonene (Carvene, Prevest DenPro Ltd. India). This process involved first writing the names of the solvents to be used i.e., Chloroform (VWR Chemicals BDH, France), Eucalyptol (Silver Bird Eucalyptus oil, Bells, Sons & Co. United Kingdom), and D-limonene (Carvene, Prevest DenPro Ltd. India) on slips of paper, scrambling them up, and putting them in a bowl. With the operator's eyes closed, a slip of paper was picked from the bowl. The name of the solvent on the piece of paper (Chloroform) was assigned to group one. The second solvent (Eucalyptol) was assigned group two, and the third solvent (D-limonene) was the third group. At the end of the allocation, each solvent group comprised of eight maxillary central incisors and six maxillary lateral incisors.

The crowns of the teeth were sectioned to obtain a uniform length of 18mm from the apex to standardize the root lengths. Removal of the residual coronal Glass Ionomer Cement was done with a high-speed round diamond bur. Removal of the coronal 2-3mm of gutta-percha within the canal to create a reservoir for the root canal solvents was done using sizes 1 and 2 Gates-Glidden burs (Henry Schein, Switzerland).

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Two drops (10µL each) of the selected solvent were placed in the created reservoir. The same dropping pipette was used for all three solvents to ensure the same amount of solvent was delivered each time.

The solvents were left in the created reservoirs for two minutes to allow the solvent to wet the surface of the gutta-percha adequately, soften the gutta-percha and percolate down within the canal. A crown-down instrumentation technique was used to remove the gutta-percha from the root canals, starting with a size 50 K-file. When the resistance to the progress of the file was encountered, the canal was irrigated and the next lower file was used to remove the GP. Debris from filing and softened GP were rinsed out using 2.5% sodium hypochlorite with a side-vented 27-gauge needle. During this process, the solvent was replenished as required.

Filing to clean the walls with the K-files followed by irrigation and replenishing of the solvent continued until there were no more gutta-percha particles on the flutes of the file. A pair of magnification loupes (3.5X, Aries Outlet, China) was used by the operator in examining the file to ensure there were no traces of gutta-percha present on the flutes. The canal was then irrigated with 17% EDTA, (Prevest DenPro Limited, India) and a final irrigation of the canal was done with 2.5% sodium hypochlorite. After complete removal of the gutta-percha from the root canals of the teeth, longitudinal grooves of 1mm depth were prepared on the labial and palatal surfaces of the teeth with a diamond bur and separating discs (NTI-Kahla GmbH, Germany) in a laboratory handpiece (Foshan Tuo Kang Medical Instruments Co., Ltd. Guangdong, China) was used to divide the teeth longitudinally.

The sectioned halves were then placed into labelled Eppendorf vials. The sectioned halves were attached to a conductive carbon adhesive tape to enable the samples to adhere to stud holders which were then mounted on a SEM specimen holder. Seven samples at a time were attached to individual studs and mounted on the SEM specimen holder. The specimen holder with the attached studs was then placed in a vacuum chamber in a sputter machine (Quorom Sputter Coater, UK). The chamber was filled with an inert gas (Argon) at 0.5 mbar for thirty minutes. The samples were sputtered with a thin layer of gold-palladium at a current of 10 mA for 3 minutes. Argon was used to prevent the gold-palladium alloy from reacting with any other element in the chamber. The gold-palladium coat enhanced the production of secondary electrons by the samples. The specimen holder with the gold-palladium coated samples was then transferred to the high vacuum sample chamber of the SEM machine (EVO MA15, ZEISS, Oberkochen, Germany). The samples were then positioned properly for the maximum effect of the primary beam of electrons. After a vacuum was generated, the samples were viewed under a magnification of X2500 that corresponded to an area of 9845.165µm^2.

For evaluation purposes, the samples were digitally divided into cervical, middle, and apical zones. The central region of each zone was located digitally and a SEM micrograph was taken (Figures 1, 2, and 3). The number of unfilled dentinal tubules per unit area was quantified using the ImageJ software (National Institutes of Health and the Laboratory for Optical and Computational Instrumentation (University of Wisconsin), United States of America).

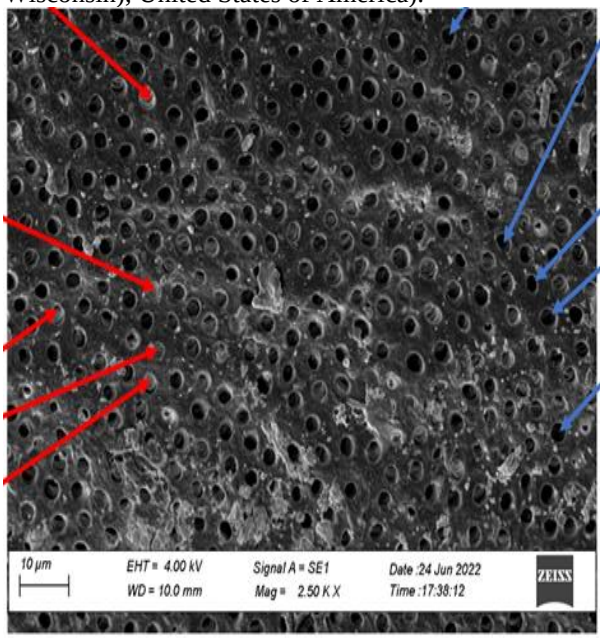

Figure 1: A scanning electron micrograph of the apical third of a root canal treated with Chloroform. Blue arrows show unfilled dentinal tubules. Red arrows show filled dentinal tubes.

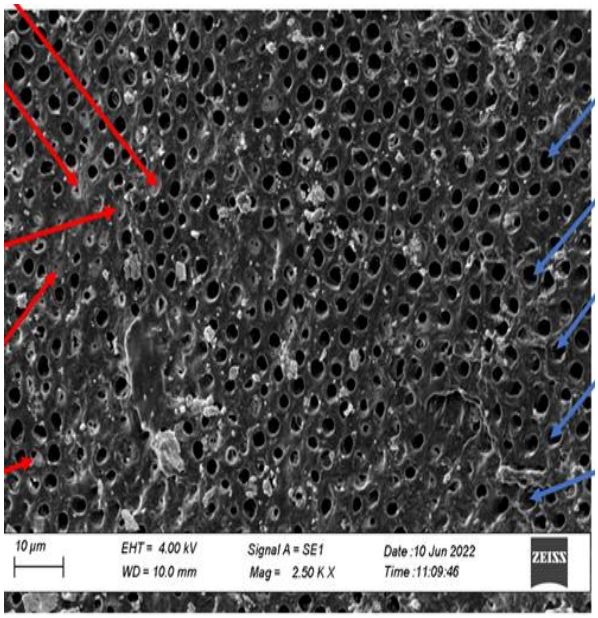

Figure 2: A scanning electron micrograph of the apical third of a root canal treated with Eucalyptol. Blue arrows show unfilled dentinal tubules. Red arrows show filled dentinal tubes.

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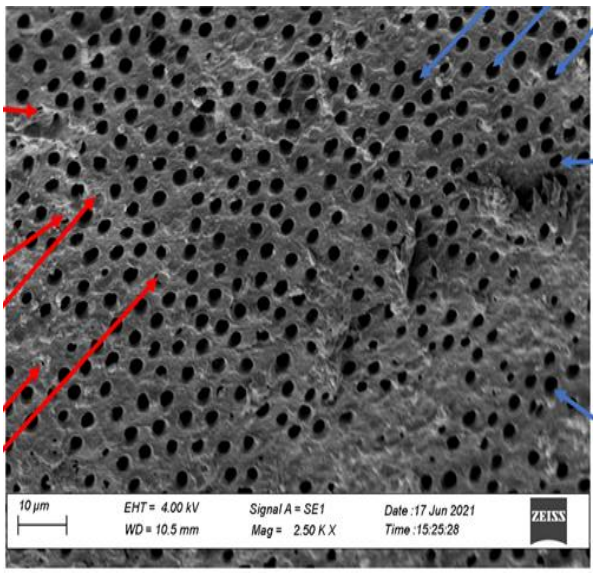

Figure 3: A scanning electron micrograph of the apical third of a root canal treated with D-limonene. Blue arrows show unfilled dentinal tubules. Red arrows show filled dentinal tubes.

Data Analysis

The Statistical Package for Social Sciences (SPSS) Version 22 was used to analyse the results statistically. The medians of the unfilled dentinal tubule orifices of the three solvents (Chloroform, Eucalyptol, and D-limonene) in the three distinct root canal parts (coronal, middle, and apical) were compared using the Kruskal-Wallis test. The level of significance was set at $p < 0.05$.

Ethical Considerations

Ethical approval was obtained from the Ethics and Protocol Review Committee of the Korle Bu Teaching Hospital (KBTH-STC 00093/2021). Written permission was obtained from the Clinical Director of the University of Ghana Dental School to use teeth from the school's Tooth Bank.

Results

Comparison of the Unfilled Dentinal Tubules Between Solvent Type for Each Tooth Segment

Using the Kruskal-Wallis test with the level of significance set at 0.05 , there was a significant difference in the median numbers of dentinal tubules free of gutta-percha in the coronal third (p= 0.007), middle third (p= 0.004), and apical third (0.001) of the teeth treated with the different solvents.

Discussion

SEM Comparison of the Different Tooth Segments

SEM analyses in each of the segments of the divided teeth (coronal, middle, and apical third) showed there were significant differences in the number of unfilled dentinal tubules among the tested solvents (Table 1.0). Across the three tooth segments, D-limonene was the solvent with the most unfilled dentinal tubules. Chloroform was the solvent with the least unfilled dentinal tubules across all three tooth segments. In this study, D-limonene and Eucalyptol were found to be better solvents for the softening and removal of gutta-percha across the length of the tooth as compared to Chloroform. In a similar study by Scelza et al.[23], although D-limonene had the most number of unfilled dentinal tubules per mm^2 in the middle and apical thirds (6332.35/ 3552.05) compared to Chloroform (6160.46/ 3575.53) and Eucalyptol (6286.96/ 3501.29), there was no statistical significant differences ($p>0.05$) in the cleaning abilities of the three solvents. These findings differ greatly from the current study where significant differences were obtained in the coronal, middle, and apical third of the teeth with D-limonene having the greatest number of unfilled dentinal tubules and Chloroform having the least number of unfilled dentinal tubules. The difference might be attributed to the fact that in the Scelza study[23], a predetermined time of 5 minutes (300 seconds) was set for each solvent so it is possible the gutta-percha was not completely removed

Table 1.0: Comparisons of the median values of the numbers of unfilled dentinal tubules in the different segments of the divided teeth across solvent groups

Tooth Segment	Solvent	Median numbers of unfilled dentinal tubules (50/ numbers)	Interquartile Range (25-75/ numbers)	p-value
Coronal	Chloroform	79.00	35.75-102.00	**0.007***
	Eucalyptol	128.00	91.00-160.25	
	D-limonene	134.50	94.75-236.25	
Middle	Chloroform	62.50	25.50-100.50	**0.004***
	Eucalyptol	107.00	51.75-147.75	
	D-limonene	149.50	96.25-190.75	
Apical	Chloroform	37.00	22.25-52.75	**0.001***
	Eucalyptol	62.00	50.00-166.25	
	D-limonene	99.50	65.50-119.50	

***and bold indicate statistically significant difference using the Independent Kruskal-Wallis test ($p<0.05$)**

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from the root canals, while in our study, removal of the gutta-percha continued until no gutta-percha remnants/ debris was visibly present on the file. The time for the complete removal of gutta-percha varies for studies. In a study by Imura et al.[2], a predetermined maximum time of 20 minutes (1200 seconds) was set for the removal of gutta-percha. However, in a study by Kasam et al.[10], no time limits were set. The mean retreatment times in that study were between 261 seconds to 523 seconds for the various solvents used.[10] No time limits were set in this study to simulate a clinical setting, where all gutta-percha must be removed from the root canal before it can be reshaped and refilled.

In the current study, the obturated teeth were left in normal saline at room temperature to simulate intraoral conditions for a period of 3 months. The storage time of the teeth varied in studies from periods of between 1 to 2 weeks to 2 to 3 months.[2,23, 24,25] A longer period of 3 months was used in this study because anecdotal evidence by the authors of this paper based on their years of clinical practice, has shown that for gutta-percha that is laterally condensed, it is possible in some cases, to remove the gutta-percha whole/ as an intact piece after about 1 to 2 weeks.

In this study, the apical third had the least dentinal tubules free of gutta-percha compared to the middle and coronal thirds. This is similar to results obtained by Scelza et al[23] and Horvath et al[25] in studies done in Brazil and Germany respectively. The reason for this could be that anatomically, the density of dentinal tubules decreases from the coronal to the apical segments of the tooth[26,27] so fewer dentinal tubules (filled or unfilled) are expected at the apical third of the root compared to the coronal and middle thirds. Another reason is that anatomically, the root canal narrows as it approaches the apex. This narrowing promotes the accumulation and compaction of debris in the apical third of the root canal if recapitulation isn't done during treatment resulting in more filled dentinal tubules. A third reason is that there is better adherence of the gutta-percha to sealer and the dentinal walls in the apical third of the tooth because the master cone fits snuggly in the apical third. Adequate quantities of the solvent might not reach these apical regions of the tooth to soften the gutta-percha. The lower number of unfilled dentinal tubules in the apical region is consistent with studies that have demonstrated that despite which gutta-percha removal technique is used, the apical third of the root canal is the least instrumented part of the root canal system.[28,29,30]

Hovarth et al[25] who also obtained their teeth from a tooth bank, postulated that the dentinal tubules in the apical third of the roots might have been sclerosed since the ages of the samples were not known. In a study done in Switzerland by Paque et al[31], they concluded that tubular sclerosis in the apical part of the root canal could account for the lesser numbers of unfilled dentinal tubules in their study. Since the ages of the extracted teeth were not known in the present study, dentinal tubular sclerosis might also account for the lesser numbers of unfilled dentinal tubules in the apical region. Another reason for the higher efficacy of D-limonene across all the tooth segments might be because D-limonene is a non-polar solvent,[18] its molecules might be able to penetrate the non-polar gutta-percha molecule more effectively than Chloroform and Eucalyptol. It also has the additional benefit of dissolving zinc oxide filler materials which account for 59.1% to 75.3% of dental gutta-percha,[14,15,16] so it is able to soften and dissolve most of the zinc oxide filler material which makes it easier for gutta-percha removal.

The main limitation of this study was the high cost of SEM scanning the eighty-four divided tooth samples. Further studies will be needed to be conducted on a larger sample size.

Of the three solvents, Eucalyptol is the most readily obtained on the Ghanaian market. Though D-limonene has more desirable properties, only a few dental supply companies stock it. Compared to Eucalyptol, the initial purchasing cost is more expensive but since fewer drops will be required per procedure, it might last longer than Eucalyptol and in the long term and might prove be more cost-beneficial.

Conclusion

D-limonene had the greatest number of unfilled dentinal tubules across all three tooth segments as compared to Chloroform and Eucalyptol. and is therefore recommended for use in endodontic retreatment. Further research on a larger sample size will however need to be done.

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Data Availability

Data is available upon written request to the principal investigator.

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EXPLORING KNOWLEDGE, BELIEFS, AND MISCONCEPTIONS ON BREAST CANCER IN AN URBAN FISHING COMMUNITY IN GHANA -A QUALITATIVE STUDY

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Abstract

Objective: This study set out to understand the beliefs of an indigenous population and explore the reasons behind this delayed presentation.

Methodology: This qualitative study adopted a cross-sectional design and was carried out in Jamestown, Ghana. The participants included opinion leaders and ordinary community members. Four focused group discussions (FGDs) and six key-informant interviews (KIIs) were conducted. A general inductive approach was used to analyze the data. Transcripts of interviews were coded in line with the developed codebook.

Results: A total of 46 participants aged 18-70 years were enrolled in this study comprising six key informants and 40 FGD participants. The median age of the key informants was 47.4 years and that of the FGD participants was 39.1 years. Females constituted 45.7% of all participants. The main themes that emerged for causes of breast cancer were; sexual fore play, exposures (risky practices), infections and "at risk groups". "Breast changes" was the main theme for presentation of breast cancer while stigma, fear, support systems, religion and attitude of healthcare workers were the dominant themes that influenced care seeking behaviour of participants.

Conclusion: The people of Jamestown had some misconceptions regarding the causes of breast cancer. They also had some knowledge about the signs and symptoms of breast cancer. They believed that early diagnosis and prompt treatment could improve the outcome of breast cancer but fear and stigma associated with the condition prevented affected individuals from seeking care early.

Key words: *Jamestown, breast cancer, qualitative study, misconceptions, knowledge*

Introduction

Breast cancer is a major public health problem that calls for collective approaches, to address the challenges[1,2]. Globally, breast cancer remains one of the most commonly diagnosed cancers in women and the leading cause of cancer-related death for women[3]. In sub-Saharan Africa (SSA), it has become the leading cause of cancer death among females[3,4,5]. Global trends have demonstrated incidence and mortality trends have decreased in developed countries in the past two decades as a result of breast screening programs and early detection[6]. However, in SSA, the incidence of breast cancer is rising due to inadequate awareness of the disease[7]. Studies in Ghana have reported a rise in incidence of breast cancers occurring in women age less than 40 compared to high-income countries where the average age at diagnosis is between 50 to 69 years[8,9,10].

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Moreover, studies in SSA demonstrate a larger percentage of aggressive breast cancer tumor subtypes than seen in other populations [11,12]. Access to care is quite complex and is influenced by patient level of breast cancer awareness, beliefs, misconceptions, lack of coordinated multidisciplinary care, low socioeconomic status, and geographic barriers[13,14,15]. As a result, breast cancer management in SSA and other low-and middle-income countries is faced with several challenges given that diagnosis at a more advanced stage often requires more resources, is more expensive, and outcomes are poorer[5,6,7,12].

The 5-year breast cancer survival rate is 40% in developing countries such as Ghana compared to over 90% in most high-income countries[16]. Early detection of breast cancer has a great impact on morbidity and mortality with a high chance of survival[17]. There are numerous factors that impact poor survival and late presentation is a major factor[10]. Delay in treating breast cancer may arise from patient delay or health system delay[11]. In many communities, late presentation stems from society-specific cultural beliefs and assumptions. As a result, interventions to promote earlier diagnosis must be tailored for each community, taking into consideration regional beliefs[12]. This study therefore

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sought to explore knowledge, beliefs, and misconceptions of the people living in an urban fishing community, Jamestown.

Materials and Methods

Study Design

To explore the knowledge, beliefs, and misconceptions surrounding breast cancer in the Jamestown community, a community-based, cross-sectional, qualitative approach was employed. Data was collected through focus group discussions (FGDs) and key informant interviews (KIIs). Field data collection was conducted in December 2021.

Study Area

This study was carried out in Jamestown, a traditional, urban, fishing community located in the center of Ghana's capital, Accra. Accra has a population density of 1,300/m^2, and Jamestown is equally densely populated (Fig 1). Jamestown has two electoral areas with one serving as the hub of the area's fishing industry and the other being more residential. There is a mix of religious, political, social, and economic classes in this area and a large indigenous population. Jamestown therefore represents a microcosm of the Ghanaian society, mirroring traditional values and beliefs. Furthermore, Jamestown is in very close proximity (2 km) to Korle Bu Teaching Hospital (KBTH) which serves as one of two tertiary referral centers for breast cancer cases offering the most comprehensive breast cancer care in the country.

Study Participants and Interviews

To qualify for participation in the study's focus group discussions (FGDs), participants were required to be adult residents of Jamestown, age 18 years or older, who were able to give consent. Two FGDs were conducted in each of the two electoral areas in Jamestown for a total of 4 FGDs. In each electoral area, there were separate male and female discussion groups. This was to enable the research team explore thoughts on the subject matter from all segments of the community. Participants for the FGDs were recruited with the help of the community leaders. Each FGD was comprised 10 participants and lasted between 35 to 50 minutes.

A total of six key informants were also interviewed. These key informants were leaders within the community and included the Chief of Jamestown (who was represented by the "Mankralo"- the Chief Kingmaker), the Queen Mother of Jamestown (who is the leader of the women in Jamestown), the traditional Chief Priest (the custodian of the customs and traditions), the Assemblyman (a political leader) and two religious leaders (one representing the Christian faith and the other representing the Islamic faith given that these are the dominant religions of the area). Both religious leaders were also community leaders who serve on the Jamestown Council of Elders where they represent the interests of their respective faiths.

A FGD guide and an interview guide containing standard questions and prompts were used for all the FGDs and KIIs respectively. All interviews and discussions were recorded using a digital voice recorder. Areas covered by the discussions and interviews included knowledge on breast cancer, causes of breast cancer, disease prevention, treatment modalities and misconceptions regarding breast cancer. Most of the discussions and interviews took place in the local language (Ga) and therefore the audio files were translated into English and transcribed by two independent translators and reviewed by a consultant well versed in both languages. Areas of disagreement were resolved by consensus.

Ethical Clearance and Consent

The study protocol was reviewed and approved by the Korle Bu Teaching Hospital Institutional Review Board (KBTH-STC/IRB/00099/2021). Written informed consent was obtained from all participants and research was conducted in line with standard research ethical principles. To ensure confidentiality, no participants' identifying details (names) were used on any form or in reports.

Data Analysis

A general inductive approach was used to analyze the data in order to achieve our a priori objective of exploring the beliefs, knowledge, and misconceptions related to breast cancer in Jamestown. This approach was used because it provided a convenient and efficient way of analyzing the qualitative data collected. An overall coding scheme was constructed with more general, upper-level categories defined by the aim of the evaluation: identifying key beliefs, knowledge, and misconceptions regarding breast cancer. More specific, lower-level codes were created from the statements presented in the raw transcribed text. Transcripts for interviews conducted with participants were received on a rolling basis and were coded in line with the developed codebook. Discrepancies were resolved through conversation between the two data analysts with direct consideration of the original data.

Results

A total of 46 participants aged 18-70 years were enrolled in this study. All study participants lived in Jamestown. There were six key informants interviewed and 40 FGD participants. The median age of the key informants was 47.4 years (range: 30-66 years) and that of the FGD participants was 39.1 years (37.5 years for the females and 40.8 years for males).

Regarding the causes of breast cancer, the following themes emerged; sexual fore play, exposures (risky practices), infection and "at risk groups". "Breast changes" was the main theme under presentation of breast cancer while stigma, fear, support systems, religion and attitude of healthcare workers were the emerging themes under influences of care seeking

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behaviour. The main theme under breast cancer outcomes was "early detection (Fig. 2).

Causes of Breast Cancer

Two main themes were identified in relation to the perceived causes of breast cancer: sexual foreplay and risky practices (exposures). Other themes that emerged were "infections" and "at risk groups".

(i) Sexual foreplay (oral breast stimulation)

Male participants attributed breast cancer to actions related to sexual foreplay. Some males reported a belief that breast cancer results from oral stimulation of the breast while others thought that breast cancer rather occurred from lack of oral stimulation. Most males, however, thought that breast cancer does not develop in women who allow their breasts to be orally stimulated or massaged by their partners. Many of the males who were interviewed shared the belief that they are able to remove "lumps" in the breast of their female partners through sexual foreplay and that, when not done, these "lumps" result in hardening of the breast and development of breast cancer.

"*Recently I was watching TV and they were discussing breast cancer and one of the messages was that the men should try and regularly suck the breast of their wives or partners. If that is done then your partner will not get breast cancer". Male Key Informant 1*

A female participant however, believed that 'allowing your breast to be sucked too much' could also result in breast cancer. This view was also shared by another male participant.

"I feel that if you have a boyfriend who always wants to suck your breast, you could get breast cancer." Female FGD2 P3

"I don't know but we hear that when the men over suck the breast, the breast milk can also form lumps leading to breast cancer" Male Key informant 2

(ii) Exposures (risky practices)

Majority of the participants attributed breast cancer to factors related to lifestyle and habits such as wearing tight clothing (especially brassieres) for long hours or putting items such as money or mobile phones in their upper clothing and brassieres. Other causes mentioned by participants included the use of skin lightening/bleaching creams, exposure to smoke from household cooking, alcohol consumption, and eating certain local foods such as kenkey (a meal prepared from fermented corn flour).

"*I know that when you put money by your breast in your brassier, you could get breast cancer. Also, when you grow old and you also drink alcohol*." Female FGD2 P1

"*I will say that most of the girls in this community like to bleach (lighten) their skin and some even use acid for the bleaching and I think this behaviour will not help us at all. So, there will be a time that the ages of people getting breast cancer will no longer be in the 50 years but rather in the 25 years. The girls of today are really bleaching which pose as risk factor to breast cancer"* Male FGD1 P4.

"I also hear that when you eat kenkey, you can get cancer but I don't know which kind of cancer it is." Female FGD1 P1

(iii) Infection

While some participants postulated that breast cancer was an infectious condition, others had a contrary opinion.

"*If I am diagnosed with breast cancer, it's not my actions that brought it and it's not infectious that anyone who gets in contact with me will get infected*" Female key informant 1

"*I can say it's infectious because if there are droplets from the affected breast into the bra and someone also wears it without washing the bra, she can be affected as well*" Male FGD2 P2.

(iv) At risk groups

All participants were aware of breast cancer affecting mainly middle-aged women although there was also the perception that women could be affected regardless of their age.

"There is no age group and anybody can get diagnosed with breast cancer. Recently, I know of a lady who was diagnosed and I think she is around 25 years and her breast was cut and she died like 3 months afterward". Male FGD1, P1

"First it was the elderly ones that were affected by breast cancer but now due to the environment, it can affect every age." Female FGD1 P2

Participants also had mixed perceptions relating to males getting breast cancer. Those who endorsed that men could develop breast cancer believed that this was uncommon compared to female breast cancer.

"I have heard that males can also be diagnosed with breast cancer but I don't know the ways in which they can get diagnosed with breast cancer". Female FGD1, P5

Presentation of Breast Cancer

Participants described their knowledge of how the disease presents itself.

(i) Breast changes

Both male and female participants reported changes in breast size, lumps and pain as important features signalling a diagnosis of breast cancer. Most participants were of the opinion that detecting these breast changes early is beneficial for treatment and that late detection likely result in loss of life.

"*One of the breasts will be bigger than the other. So, when you see such things, you quickly have to rush to*

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the hospital for care. But some people will not go to the hospital and before they realize, it will be too late". Male FGD2, P3

"There are several symptoms of breast cancer. The tip of the breast becomes reddish, the discharged is sluggish." Male FGD1, P2

Influences of Care Seeking Behavior

(i) Stigma

Majority of the focus groups and the interview participants acknowledged that there is a cultural stigmatization of women in the community who develop breast cancer. Some reported that some breast cancer patients stigmatize themselves and thus avoid getting close to other people for fear of being rejected. Others are stigmatized by the people around them and this manifests as rejection. Stigmatization of the condition was also related to late presentation at the health facility and was responsible for breast cancer patients not informing their family and friends early.

"You will be neglected and people will start to gossip and reject you. They want to avoid you in order not to also get affected" Female FGD2, P3

"I have to encourage her to go to the hospital for care. I don't have to neglect her else she will feel rejected." Male FGD1, P5

(ii) Fear

Fear was a common emotion that was mentioned by several participants. Whereas, female FGD participants mentioned worry and fear related to surgery of the affected breast, male participants alluded that breast cancer was dangerous and could easily result in loss of life. Some participants also attributed their fears to the outcome of breast cancer diagnosis seen in others including family members and friends while others worried about the cost of management and the financial burden that the cancer imposed on the individual and the family.

"They are afraid that if they go to the hospital, they will be told they have cancer." Male key informant 2

"My sister suffered from breast cancer and she said it started like a boil in her armpit and she went to Korle Bu Hospital for treatment. She was given medicines and was booked for surgery to remove the lumps in her breast. After the surgery they didn't see anything in her breast and they stitched it back. But after a while, the thread removed and it developed into a sore and she couldn't get better till she died. So, when I hear about cancer, I get worried a lot". Male key informant 3

"*If the treatment can be made free, that will encourage people to seek prompt care when they don't have money. There are some diseases for which treatment is free so breast cancer treatment can be made free as well. Then we could get the drugs free and we can seek early treatment"* Female FGD2, P3

(iii) Support systems

Support systems in the form of family, community and spiritual/prayer were outlined. Both female and male participants mentioned that spousal support was very important during the period. In addition, financial support was referenced as a major factor influencing delay or not seeking care for breast cancer. Male participants described their role in providing emotional and financial support for their partners during the time of treatment. Prayer was also mentioned as a way of relieving the anxiety and fear due to the condition.

Sometimes people are afraid when they are going for surgery so then we add prayers to guide them through safely" male key informant.

"When you realize that your partner or sister is diagnosed with breast cancer, you should be able to help her with the treatment. Even if she is afraid, you need to force and take her to see the doctor. If you leave your partner without supporting her, she might be having thoughts of this breast cancer and that could lead to her death. So, males play a role and must be fully involved". Male key informant

Some women seek spiritual or prayer support as part of the treatment process.

I don't see this disease as a spiritual problem but you could consult the family priest for prayers Female key informant.

The KIIs endorsed male support of their female partners in the treatment process.

"As a male, if your wife, sister or relative is diagnosed with breast cancer, you need to support the person in this condition in terms of visit to the hospital for treatment and provision of financial assistance to the person. The man needs to play a key role in the treatment process." Male key informant

In addition, female respondents believed that they can get the needed support from their male counterparts when they ask for it.

"It's mostly your brother or sister who can support you for the treatment process. Also, if it's the mother who is diagnosed with breast cancer, then the children who love the mother will support the treatment process." FGD female participant

"I will say that you should not be afraid as the man but then take your partner to the hospital for treatment" FGD Male participant

"I will give the go ahead (for surgery of the affected breast) if that will help save her life. Male key informant

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(iv) Religious Influence of Care

One of the considerations for some women seeking care for breast cancer was the religious interplay. Specifically, there was a preference of "faith-based" medical care providers, care provided by health care professionals of their same religious background, and a preference for female nurses and doctors amongst Islamic patients.

"As a Muslim, we have a lot of problems as to how and when our women are being treated. Majority of the Islamic women would like to be treated by a fellow Islamic woman. This is because our religion does not approve of any other man seeing the nakedness of a woman apart from her husband. Unfortunately, we don't have it that way. The only recognized Islamic clinic that we have is Iran clinic." male key informant 6

"So, if you give them that assurance in a meeting or forum that female nurses or doctors will be provided to take care of them, then that will be well accepted by all" male key informant 6.

(v) Attitude of healthcare workers and long waiting times

Some participants complained about the attitude of some healthcare workers and indicated that it was the reason why some patients reported late or refused to seek help at healthcare facilities. The long waiting times before one can see a doctor was also mentioned as a factor that influences health care seeking behaviour.

"Delays by the care providers: I am saying this because my sister delivered at Korle Bu hospital and we had to get blood for her. So, whiles waiting a patient was brought in but the nurses sat there chatting unconcerned" Male FGD1, P5

"At times when we are sick and need to see a doctor, you think about the long waiting time that we spend at the hospital and will rather want to buy drugs at the pharmacy and take. But we are advised not to just walk into pharmacy and buy drugs. Maybe the person is an apprentice working with someone and cannot stay all day at the hospital seeking care. So, then she will buy drugs at the pharmacy and take. So, the doctor and nurses should work on the long delays at the hospital." Female FGD2, P3

Breast Cancer Outcomes

Participants expressed the fact that early detection saves lives. They mentioned that the factors contributing to
delays in seeking early care were multifaceted including attitude of some care providers and individual's delay/denial of the disease condition.

"But the good thing is that, when you seek early care at the hospital, the doctors will know the stage of the disease and provide the needed care for you before it gets to the worse stage". Male key informant

"*It's not always about the money because in my sister's case, we had the money but then maybe she had the condition long ago but didn't voice out early and it was when things got to the worse stage that she voiced out and we rushed her to the hospital. Just two weeks afterwards, her breast was cut off". FGD,* male participant

Breast Cancer Treatment

The participants described several treatment/control options available to persons diagnosed with breast cancer. The main treatment options mentioned were surgery (mastectomy) and use of medications. Some participants have heard of herbal or local remedies but are not certain of the validity of these cures.

"*Yes, every disease has cure for it but then when you discover it early then treatment is given on time*" male key informant 3.

"*No, but I heard a man selling drugs in a bus who said there is herbal treatment for cancer. He showed some herbs that can be used in addition with shea butter and applied on the affected breast. But as to whether what the man was saying in the bus was true or not, we cannot tell. But then we don't have any local herbal treatment for breast cancer in this community*". Female FGD1, P5

"*If she goes to the hospital early for care and she is given medicines for treatment, I think it will help than delaying to getting it worse off to the point of cutting*". Male key informant 4

Breast Cancer Prevention

There has been support for the breast cancer awareness month held in October every year, however there were concerns that these educational programs are not sustainable and most end with the month-long campaign on breast cancer in October every year. Participants called for educational programs from time to time to improve awareness of breast cancer. Individuals believe that through more education to the community outcomes will improve for women diagnosed with breast cancer.

"When these celebrations are over then that is all. Last month when we planned to have the breast screening as part of breast cancer awareness day, the people in the community were not even aware of the occasion and we had to go round in the community with megaphone to create awareness before people came. After the celebration of the day, there isn't enough education. So, there is no sustained education after a health event. The frequent education will help the community to be updated on health issues and how to prevent or get treatment". Male key informant

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"We need to educate our wives to avoid the causes of breast cancer". Male FGD1, P1

"We can also educate our sisters, other females we know on those things that cause breast cancer. Male FGD2, P5

Discussion

Perceived Causes of Breast Cancer

From the findings of both the focus group discussions and key informant interviews, the perceptions of the participants on the causes of breast cancer were quite different from the thoughts of participants of a qualitative study on breast cancer carried out in rural Northern Ghana in 2010[1]. In that study, the participants had poor knowledge of the aetiology and risk factors of breast cancer, especially considering they did not even have local terms to describe breast cancer. Again, participants of that study, who were homogenously female, had a perception that breast cancer risk (especially the type they categorized as chronic) was related to women having large breasts and being either slim or obese. These thoughts were quite different from that of the participants in our current study more than ten years later, who thought the risk for breast cancer was related predominantly to either sexual foreplay involving the breasts (or the lack of it), or putting money and other foreign materials close to the breast. The difference in findings could have been from a variety of factors such as changing times (that is, information availability and accessibility over the years), the rural-urban setting difference or even the differences in the gender constitutions of the participants of both studies. On the other hand, a survey carried out on some Ugandan women (aged 25 years and above), found the beliefs of women on the cause of breast cancer to be similar to what the participants of our study expressed. In their 2014 survey, 47% of their respondents were of the belief that putting items in the brassier was a cause of breast cancer and this opinion was significantly associated with no previous education on breast cancer, emphasizing the importance of proper education on important health issues such as breast cancer[21].

A cross-sectional study in rural and urban Ethiopia assessing knowledge of young women on the risk factors of breast cancer showed that nearly 82% of the participants had low awareness on the risk factors of breast cancer[17]. This finding corroborates our findings of low knowledge of the actual causes of breast cancer in our cosmopolitan area of study, even though our study had participants of varying ages and gender.

Knowledge and Experience of Breast Cancer Symptoms

None of the participants of the interviews and discussions were survivors of breast cancer, however, some had some second or third hand experience of the disease through relatives and acquaintances. Their view that though breast cancer affects mostly the middle aged, people of all ages were at risk was similar to the view of the Ugandan women who participated in a survey assessing beliefs on breast cancer[17].

The mixed perceptions of the occurrence of breast cancer in males were not unique to our participants. Even among male relatives of women who have had breast cancer, there seems to be low awareness of men being at risk of breast cancer[22]. A more recent quantitative study in 2018 among male university students in Brazil also yielded similar findings, that awareness of breast cancer occurrence in males was poor[23]. And this finding was independent of the area of study (health, sciences, or humanities) of these students. If students of health sciences have low knowledge on breast cancer in males, then there is indeed a large knowledge gap that must be filled.

Even though most of the participants in our study had mixed perceptions about breast cancer in males, the same cannot be said about their knowledge regarding symptoms of breast cancer. They all agreed that the common symptoms of breast cancer were breast lumps, pains and changes in breast size. They however demonstrated inadequate knowledge regarding early presentation and diagnosis. In agreement with the review of barriers to early presentation and diagnosis of breast cancer among African women, carried out by Akuoko et al.[24], the urgency and necessity of improving education and knowledge dissemination among the members of the Jamestown community and beyond, cannot be overemphasized[24].

In addition, when the subject of breast cancer being infectious came up, our participants had dichotomous views. Some said breast cancer was not infectious, while others thought sharing an unwashed brassiere can result in breast cancer transfer, similar to the thoughts of the Ugandan women in the survey, who said wearing dirty second-hand bras could cause breast cancer[21].

Stigma and Fear

From the discussions with our participants, stigma and fear were two major barriers of health seeking for early diagnosis and intervention where breast cancer was concerned. These findings are in agreement with other studies[24]. In the study by Akuoko et al.[24] women with breast cancer feared being ostracized by their families because of their health condition[24]. Participants in our current study however were of the view that people may delay in seeking help because of fear of being stigmatized by their own families.

Even when it came to discussing fear related to breast cancer, the men in our study groups had a different view to what the women thought; the men were more concerned about the potential loss of life associated with breast cancer while the women were more concerned about loss of the breast through surgery. These fears and others highlighted in the results seem to be common to people who have to deal with the threat of breast cancer as referred to by eight of the publications reviewed by Akuoko et al.[24] As these fears are common and not localized, education on breast cancer must intentionally

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be engineered to allay the fears of people as much as possible so as to improve health-seeking behaviour and outcomes in cases of positive diagnosis.

Other Barriers to Health Seeking

Aside fear and stigmatization, the other barriers to health seeking in cases of suspected breast cancer identified by participants included financial constraints and poor attitude of some healthcare professionals.

One noticeable thing was that participants in this study did not mention alternate sources of treatment (particularly herbal or spiritual) as a natural preference for some people faced with fearful conditions like breast cancer unlike what was explained by the findings of a study by Opoku, Benwell and Yarney (2012) in Accra and Kumasi- two urban cities in the Ghana[25]. Other findings of that study on the barriers of health-seeking were similar to what our participants reiterated; unsupportive healthcare systems, financial constraints, fears and stigma[25].

Support

There seemed to be a consensus on the necessity of support for victims of breast cancer among our study participants- both males and females. From their views, they expressed willingness to support should they have to, and even convince or "force" the victims to seek health care if necessary.

Support structures are needed in the healing and recovery process. Spousal support was outlined as a vital role in the treatment process. Of note were family support as well as emotional and financial support from husbands and this is supported by a Ugandan study involving breast cancer survivors, who affirmed the importance of family support in their healing and survival process[20].

Conclusion

The people of Jamestown had some misconceptions regarding the causes of breast cancer; they believed that keeping money and other items in the brassieres could cause breast cancer. They also believed that sexual foreplay, particularly the sucking of the breast was associated with breast cancer. They also had some knowledge about the signs and symptoms of breast cancer. They believed that early diagnosis and prompt treatment could improve the outcome of breast cancer but fear and stigma associated with the condition prevented affected individuals from seeking care early enough.

Recommendation

This study identified one key factor that requires health system strengthening and that is the request for female clinicians to address the health needs of female Islamic women. The inadequate presence of female clinicians at health facilities has inhibited the seeking of care by some Islamic women in Ghana. This calls for pragmatic collaboration among faith-based healthcare providers to design interventions to bridge such gaps and create the grounds for healthcare for all women in Ghana.

Secondly, education and awareness creation on breast cancer should not be limited to the month of October which has been set aside as breast cancer awareness month. Rather, The Ministry of Health, Ghana Health Service and their partners should work towards achieving and maintaining an all-year-round education and awareness creation on breast cancer to sustain the gains made during the month of October (which is dedicated to breast cancer awareness creation).

Data Availability

All data for this study may be found at https://doi.org/10.6084/m9.figshare.25195583.v1

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STRESS AND BRUXISM: A STUDY AMONG DENTAL AND MEDICAL STUDENTS AT THE UNIVERSITY OF GHANA

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Abstract

Objective: This study aimed to determine the association between stress and bruxism.
Methodology: A cross-sectional study was done among dental and medical students of the University of Ghana. Anonymized online questionnaires were distributed to the target population. Participants were asked if they, or anyone had noticed them repeatedly grind or clench their teeth while sleep or awake. The questionnaire also included the Perceived Stress scale (PSS) to determine the levels of self-perceived stress among the participants. The presence or absence of bruxism was cross-tabulated with the levels of PSS scores.
Results: A total of 129 students participated in this study. These consisted of 70 females. The prevalence of self-reported bruxism in general was 8.5% in the study population. That of sleep bruxism was 5.4%, while awake bruxism was self-reported in an equal number of students. The distribution of self-reported bruxism varied significantly among the different academic levels of the study participants (P=0.008). Students with bruxism reported higher stress scores (P=0.041).
Conclusion: Dental and medical students with self-reported bruxism indicated higher stress scores.

Key words: *Bruxism, stress, Ghana, parafunctional habit*

Introduction

Originating from the Greek expression "brychein odontas", Bruxism is translated to mean gnashing one's teeth[1], and represents a condition characterized by clenching or grinding of the teeth. This may be accompanied by bracing or thrusting of the mandible.[2] Several factors have been linked to bruxism. These include stress, occlusal factors, and central nervous or pathophysiological factors.[1] Broadly, the condition may manifest as sleep bruxism or awake bruxism.[2] It has been reported that particularly for sleep bruxism, events follow a certain notable autonomic activities of rapid-frequency cortical electroencephalogram (EEG) activity, heart rate elevation, increased jaw and oropharyngeal muscle tone, and increased respiratory effort and nasal air flow, leading to an elevated rhythmic masticatory muscle activity in the jaw muscles.[3,4] Bruxism may lead to headaches[5], muscular pain around the jaws and temporomandibular joint[6], and worsening pre-existing periodontal disease[7]. It may also cause damage to restorative work, and for denture wearers, lead to pain and soreness of the denture bearing mucosa.[8]

Bruxism is considered to be a fairly common parafunctional habit, with worldwide reports of prevalence range from 8% to 31% in the general population.[9] It is also reported to affect 15 to 40 percent of children and 8 to 10 percent of adults.[3] The incidence of bruxism amongst different ethnic groups also varies. In a study conducted on students of four ethnic groups, distributions were evidently different. African-American students reported the lowest incidence of self-reported bruxism (9.4%), Asian students the highest incidence (24.6%); Euro-American and 225 Hispanic students' incidence were intermediate.[10]

There seems to be scarce reports on the condition in Ghana and its subregion, while literature does not give any conclusive evidence on the relationship between bruxism and stress. This study, exploring self-reported bruxism and perceived stress, reports the prevalence of the condition and relationship with stress, among the unique population of dental and medical students.

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Materials and Methods

Study Design and Participants

For this study, we carried out a cross-sectional study among dental and medical students of the University of Ghana from May to June 2021. Anonymized online questionnaires were distributed to the target population over the study period. The questionnaire (unvalidated) included questions on socio-demographics, and sought to determine the presence of self-reported bruxism. The study included current medical and dental students of the University of Ghana. Enrolled students who had not begun academic work were excluded. Pre-clinical Graduate Entry Medical students were also excluded from the study. Participants were asked if they, or anyone had noticed them repeatedly grind or clench their teeth while asleep (night bruxism) or awake (awake bruxism). Furthermore, they were asked if they experienced trismus, soreness or fatigue of the jaw or

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temporal region on waking up. The questionnaire also included the Perceived Stress scale (PSS) to determine the levels of self-perceived stress among the participants.[11] The scale required participants to answer 'never', 'almost never', 'sometimes', 'fairly often', or 'very often' to ten questions describing stressful events in the past month.

Ethical Consideration

Ethical approval was obtained from the Ethical Review Committee of the University of Ghana College of Health Sciences (ERC: CPDD/009/011/2020).

Data Analysis

Returned questionnaire were checked for errors. Incomplete questionnaires were excluded from the study. Collected data were entered into Stata software Stata (16.1, Stata Corp LLC, College Station, TX) for analyses.

The prevalence of sleep and awake bruxism among the study population were determined. The PSS scores were obtained by reversing responses (e.g., 0 = 4, 1 = 3, 2 = 2, 3 = 1 & 4 = 0) to the four positively stated items (items 4, 5, 7, & 8) and then summing across all scale items. Total scores were obtained for all participants. The median scores were obtained for the entire population and sub-populations based on the sociodemographic variables. Scores were further divided into 'low', 'moderate' or 'high' levels of stress for scores corresponding to '0-13', '14-26', and '27-40' respectively. The presence or absence of bruxism was then cross-tabulated with the levels of PSS scores, applying the Chi-square test and Fisher's exact test where applicable. The mean PSS scores were also compared among background characteristics. The 'medium' and 'high' PSS levels were further classified as 'substantial' stress. The distribution of 'substantial' stress was determined among sex, course of study, and level of study.

Results

A total of 129 students participated in this study. These consisted of 70 females. About a quarter of the study population were made up of dental students. Other background characteristics are shown in Table 1.

The prevalence of self-reported bruxism in general was 8.5% in the study population. That of sleep bruxism was 5.4%, while awake bruxism was self-reported in an equal number of students. Three participants (2.3%) gave the indication of experiencing both awake and sleep bruxism. The distribution of self-reported bruxism was significantly distributed among the academic levels of the study participants (P=0.008).

The Perceived Stress scale scores ranged from 0 to 36, with mean and median scores of 18.9 (SD= 7.8) and 19 (IQR: 14,23) respectively. The mean PSS scores varied significantly among sex, study course, level, and age category. Furthermore, participants who indicated experiencing bruxism had significantly higher scores compared to those who did not experience bruxism (P-value=0.041). There was generally a high prevalence of 'substantial' stress among the study participants, being present in 99 (76.7%). This was not significantly distributed among the various sub-populations (Table 3).

Table 1: Background Characteristics of Respondents

Variable	Number	Percent
Sex		
Male	59	45.7
Female	70	54.3
Course		
Dentistry	34	26.4
Medicine	95	73.6
Level		
Basic Science	12	9.3
1st Clinical	18	14.0
2nd Clinical	21	16.3
3rd Clinical	26	20.2
Final year	52	40.3
Age Category		
Less than 23	59	45.7
23 or more	70	54.3

Table 2: Distribution of Bruxism among dental and medical students

Variable	Day Bruxism	Night	Total	X^2 (P Value)
Sex				
Male	4 (5.8)	4 (6.8)	7 (11.9)	0.343
Female	3 (4.3)	3 (4.3)	4 (5.7)	
Course				
Dentistry	1 (2.9)	2 (5.9)	3 (8.8)	0.943
Medicine	6 (6.3)	5 (5.3)	8 (8.4)	
Level				
Basic Science	1 (8.3)	0	1 (8.3)	0.008
1st Clinical	0	0	0	
2nd Clinical	0	0	0	
3rd Clinical	3 (11.5)	6 (23.1)	7 (26.9)	
Final year	3 (5.8)	1 (1.9)	3 (5.8)	
Age Category				
Less than 23	2 (3.4)	4 (6.8)	5 (8.5)	0.984
23 or more	5 (7.1)	3 (4.3)	6 (8.6)	

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Table 3: Perceived Stress Among Participant Characteristics

Variables	Stress score (SD)	Test	Moderate/ Severe (%)	X^2 (P-value)
Sex		0.332		0.340
Male	8.3 (9.2)		43 (72.9)	
Female	19.6 (6.5)		56 (80)	
Course		0.011*		0.065
Dentistry	21.9 (6.7)		30 (88.2)	
Medicine	17.9 (7.9)		69 (72.6)	
Level		0.001*		0.274
MB 2 Class	20.1 (6.6)		11 (91.7)	
MB 3 Class	20.5 (7.4)		13 (72.2)	
1st Clinical	22.7 (7.0)		19 (90.5)	
2nd Clinical	17.6 (7.6)		18 (69.2)	
Final year	17.3 (8.2)		38 (73.1)	
Age Category		0.018*		0.145
Less than 23	20.7 (7.1)		49 (83.1)	
23 or more	17.5 (8.1)		50 (71.4)	
Bruxism		0.041*		0.456
Yes	22.9 (6.1)		10 (90.1)	
No	18.6 (7.8)		89 (75.4)	

Discussion

This study, exploring bruxism among a unique population of dental and medical students found its prevalence to be 8.5%. Of this number, 27% reported the occurrence of bruxism both at night, and while awake. The prevalence of bruxism seems to vary, largely depending on the population of study as corroborated by Strausz et al,[12] that the older the population, the lower the prevalence of bruxism. This study found 8.5% while 27% experienced both awake and asleep bruxism. For instance, Fluerasu et al,[13] recorded prevalence of 15.2% for awake bruxism while asleep bruxism was 32%. Our total prevalence of 8.5% was close to that of Wetselaar et al[14] conducted on the Danish population which revealed 6.6% for awake and 20% for asleep bruxism. From the various studies done across different geographical and cultural backgrounds, bruxism is a major challenge mostly triggered by psychological factors including stress and anxiety and manifests negatively in the dento-maxillary functions of the individuals. There is the need for extensive education to create awareness among the public on the causes of such pathology when it presents so that the appropriate remedies can be sought.

The relationship between bruxism and stress has been implied by several authors over the years. Physiologically, it has been suggested that the two processes might sometimes share some common pathways. Chemelo et al, despite the low certainty of the evidence, demonstrated that stressed individuals show a higher chance of experiencing bruxism when compared to healthy individuals.[15] In corroboration to this observation, our study showed that patients with bruxism significantly had higher stress scores.

Our study population, consisting of Dental and Medical students is generally considered to be exposed to several stressors.

From this study, dental students reported a higher level of stress compared to medical students. This observation was at variance to findings by Bali et al, who reported that stress scores for medical students were higher than those for dental students.[16] In the geographic region of the study, dental and medical students are essentially one class for the first four years of study. Among these, 1st clinical year students reported the highest stress scores. Younger students, (less than 23 years) also had higher stress scores. This could have been due to acquisition of adaptive mechanisms over time, as students grow into their fields of study.

Compared to sleep bruxism, awake bruxism is more linked with life stress caused by familial responsibility or work pressure. Sleep bruxism on the other hand is considered as a stereotyped movement disorder occurring during sleep, and classified as a sleep related movement disorder according to recent classification of Sleep Disorders.[1]

Conclusion

This study further highlights the potential interrelationship of the two clinical entities which may be relevant for medical practice. Stress management could therefore be considered as a target for allied therapy in the treatment of bruxism. Similarly, bruxism should be considered as a potential sequalae in long-standing stressful situations in the Ghanaian environment.

Our study could have benefited from a larger sample size, while the assertion of the link between bruxism and stress would need further clinical and laboratory investigations. Furthermore, future studies could also incorporate more robust designs and research variables. This study however provides useful information that could be used to inform subsequent studies in Ghana and the sub-region.

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REVIEW ARTICLE

CARDIOVASCULAR DISEASES, MEDICATION NON-ADHERENCE, AND THE POTENTIAL OF PERSONALIZED MEDICINE: A COMPREHENSIVE REVIEW

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Summary

Non-communicable diseases (NCDs) account for approximately 73% of global deaths, with cardiovascular diseases (CVDs) as the leading cause. It was responsible for 17.8 million deaths and significant disability-adjusted life years (DALYs) worldwide in 2017. In Africa, CVDs represent 38.3% of the NCD burden, and their incidence has surged by 50% over the past three decades, with sub-Saharan Africa experiencing the highest global burden of stroke. Medication adherence is a critical factor in managing CVDs, yet adherence rates remain alarmingly low, particularly among cardiovascular patients, where over 60% do not adhere to prescribed treatments. This review explores the importance of medication adherence in CVD management, the emerging role of personalized medicine, and genetic influences on adherence behaviours. Personalized medicine, which uses genetic, environmental, and lifestyle data for tailored healthcare, offers a transformative approach to CVD treatment, potentially improving outcomes and patient adherence. The review also examines recent advances in genomic research related to CVDs and medication adherence, highlighting the need for updated studies and innovative strategies to integrate genetic insights into clinical practice. Addressing these challenges and leveraging personalized medicine have the potential to enhance CVD management and patient outcomes significantly.

Introduction

A large percentage of global deaths, approximately 73%, can be attributed to Non-Communicable Diseases (NCDs). The leading cause of mortality within this category is cardiovascular diseases (CVDs), which encompass a range of cardiac and vascular conditions such as ischemic heart disease, stroke, heart failure, and peripheral arterial disease. CVDs have a significant impact on the quality of life. In 2017, CVDs were responsible for causing 17.8 million deaths worldwide, resulting in the loss of 330 million years of life and an additional 35.6 million years lived with disability, according to estimates. [1,2,3] CVDs are the most significant contributor to the total NCD burden in Africa, accounting for 38.3% of NCD deaths and 22.9 million DALYs. Alarmingly, there has been a 50% increase in the CVD burden in Africa within the last three decades.[4,5]

There is an unparalleled increase in the incidence, prevalence, and fatality of strokes in sub-Saharan Africa. With a population of 1 billion people on the continent, a stroke strikes someone every 6 minutes, particularly affecting the younger and middle-aged populations. Global estimates of stroke suggest that sub-Saharan Africa has the highest burden of stroke.[6,7] The burden of CVDs is also apparent in Ghana, where there has been an increase in the percentage of CVD admissions and deaths. [8]

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Importance of Medication Adherence in Managing CVDs

The World Health Organization has defined medication adherence as the extent to which an individual's actions align with the prescribed advice of a healthcare provider.[9] Non-adherence to medication is a big issue, with only about 50% of patients adhering to their prescribed medication [10] and more than 30% of hospital admissions due to medicine-related issues resulting from non-adherence.[11] The situation is worse in cardiovascular patients, with over 60%, not adhering to their medication, indicating a prevalent issue of non-adherence.[12,13] Non-adherence remains a significant challenge, particularly for patients with chronic conditions, and can lead to hospitalization and other adverse outcomes. Conversely, high adherence rates are associated with lower cardiovascular risk, highlighting the importance of addressing medication adherence issues. [14]

Drug therapy has reduced the morbidity and mortality linked to cardiovascular disease, however, non-adherence to recommended treatment has remained a major obstacle to better patient outcomes.[15] Medication adherence in cardiovascular disease has a huge prospect to improve outcomes including blood pressure control and ensuing events. As such, the American Heart

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Association (AHA)/American Stroke Association (ASA) has made a goal of improving medication adherence in CVD and stroke prevention and treatment. [16,17] A meta-analysis conducted showed that poor adherence to vascular medications contributes to a significant proportion of all cardiovascular disease events and mortality in patients with CAD. [18]

Introduction to the Concept of Personalized Medicine in CVD Treatment

Personalized medicine or precision medicine is an innovative clinical strategy that guides medical management by using personal genetic, environmental, and lifestyle data. [19] Most CVDs are caused by a complicated interaction between modifiable and non-modifiable risk factors, which exacerbates innate genomics, transcriptomics, epigenomics, metabolomics, proteomics, and microbiomics tendencies. The majority of diagnostic standards and treatment strategies in modern cardiology are based on population-based research, with less emphasis on methods designed to personalize patient care. The role of precision medicine in CVD treatment is potentially the game changer. Previously thought to be unattainable, current trends and findings show otherwise. [20] A study by Shah S et al. Revealed that loci KLHL3 and SYNPOL2–AGAP5 are implicated in HF, and also BAG3 and CDKN1A are associated with LV systolic dysfunction. Thus, medications targeting these genomes or in vitro alterations may improve clinical outcomes in these patients. [21]

Advances in genomics are helping the knowledge gained to be incorporated into the treatment and diagnosis of MI. Genome-wide association studies have identified genes associated with polygenic states such as serum LDL cholesterol levels and coronary artery disease, RCT by Scott R et al.[22] discovered six genes (CNR2, DPP4, GLP1R, SLC5A1, HTR2C, MCHR1) that could be potentially used to develop drugs to treat type 2 diabetes or obesity without incremental CVD risk.[22] Additionally, gene therapy has been investigated as a potential treatment for lipid disorders, such as familial hypercholesterolemia, which can lead to the early onset of cardiovascular disease. E.g., the development and FDA-approval of Incliseran (a small interfering RNA, siRNA, that acts as an inhibitor of a proprotein convertase, specifically, inhibiting translation of the protein PCSK9) [23,24] Several studies have shown the response of antihypertensives to certain loci. An example is SNP rs7297610 CC located on chromosome 12q15 and its association with thiazide diuretic response in African Americans. [25] An ongoing trial, the AIM HY study, is underway to investigate biochemical pathways, pharmaco-metabolomics, and pharmacogenomics in antihypertensive drug response which can further be used for precision therapy in hypertension. [20]

Genetic Predisposition to Non-Adherence Behaviours

A study by Rayner et al to examine genetic influences on treatment-related behaviours; showed substantial genetic overlap between lifetime treatment-related behaviours and psychiatric disorders, symptoms, and behavioural traits. This was based on the role of common genetic variation on four-lifetime treatment-seeking behaviours (treatment-seeking, treatment-receipt, self-help, self-medication with alcohol/drugs) examined in participants of the UK Biobank (sample size range: 48,106 - 75,322). [26]

Another study used genome-wide complex trait analysis (GCTA) to investigate the genetic component of glaucoma medication non-adherence. The findings suggested that 57% (MPR80) and 48% (PDC80) of glaucoma medication non-adherence could be attributed to a genetic component. The study also identified risk and protective statistically significant genes/pathways underlying glaucoma medication non-adherence for the first time.[27] Several studies have examined the impact of personality on medication adherence. Youn-Jung Sun et al. found that Type D personality increased the risk of medication non-adherence following Percutaneous Coronary Intervention and thus inference can be made that the genetic basis of Type D personality may be linked to medication non-adherence. [28]

Mechanisms through which Genetic Variants Influence Medication Adherence

It has been hypothesized that genetics might play a role in drug adherence through similar mechanisms such as identified by pharmacogenomic studies. These studies show several genetic variants relevant to drug response that can increase an individual's risk for adverse drug reactions and an adverse drug reaction decreases the likelihood of a patient continuing to take a medication. [29]A GWAS on a Finnish population examining adherence to 5 classes of chronic medications including statins and blood pressure medications showed established pharmacogenes such as SLCO1B1(for statins) did not associate with adherence, however, 5 SNIPS were genome-wide significant. Including rs1339882991 which positively correlated with adherence to BP medications. [30] The extent to which genetic variables contribute to the diversity in lifetime patterns of drug usage in cardiometabolic disorders remains largely unknown, despite significant advancements in the field of disease genetics. Genome-wide association studies have identified a complex polygenic architecture comprising hundreds of associated loci for lipid levels, blood pressure and T2D. [31,32] A systematic study of genetic effects on medication-use patterns using cardiometabolic medications found 333 independent loci associated with medication use. Of note, known lipid- (PCSK9, LDLR, and APOE) and blood pressure-related (WNT2B and HOXA13) loci

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were associated with discontinuation of medication use in hyperlipidemia and hypertension respectively.[33]

Sociocultural and Religious Factors as Confounders

Studies investigating the relationship between genetics and medication adherence in CVD as well as various disease conditions, such as cancer and HIV, demonstrate that genetics may play a role in medication adherence. It is important to note, however that multiple factors, such as patient attitudes toward medications, may influence this relationship.[34,35,36] The World Health Organization has identified five interrelated dimensions as barriers to medication adherence which include social and economic factors, healthcare teams and system-related factors, condition-related factors, therapy-related factors, and patient-related factors.[37] The most frequent reason for non-adherence to prescribed regimes in sub-Saharan Africa is the unaffordable cost of chronic management. Nevertheless, forgetfulness and concerns about adverse effects also play a part. The level of educational attainment and a preference for traditional medicine may also predict non-adherence [38]

A study in Ghana among hypertensive and diabetic patients found that Perceptions that the medications are ineffective for treating the diseases led to non-adherence. Due to their easy accessibility, perceived efficacy, and cost, patients with these perceptions rejected the pharmaceuticals and instead resorted to herbal remedies and spiritual healing as therapeutic alternatives. Additional factors that were shown to impact non-adherence included the practice of polypharmacy, hectic work schedules, social norms, inadequate prescription guidance from healthcare practitioners, and pharmaceutical knowledge and expertise. [39]

Clinical Implications and Applications of Genetic Insights

Advances in sequencing technologies have revolutionized genetic studies by enhancing the understanding of human genome variations and their links to health conditions. Progress has accelerated discoveries in complex diseases, such as diabetes, cancer and cardiovascular disorders and, advanced genomics and medical diagnostics. As a result, individual genome profiles now play a crucial role in precision medicine for personalized diagnosis and treatment. [40]

Pharmacogenetics data are increasingly used to guide treatment decisions for various anticancer drugs, with the Clinical Pharmacogenetics Implementation Consortium (CPIC) evaluating when and how to apply genetic information for personalized therapy. For hypertension, promising pharmacogenomic findings include two genes—NEDD4L for thiazide diuretics and ADRB1 for β-blockers—that show associations with blood pressure management and cardiovascular outcomes. Both genes were identified through candidate gene studies. [41] Traditionally, most proposed solutions to non-adherence have focused on behavioural interventions, social and economic factors, patient-related factors as well as health system-related factors. Much research has not been done on the genomics of non-adherence in cardiovascular diseases.

According to Pritchard et al, the establishment of personalized care includes overcoming challenges in these five sections, namely; Education and awareness; Patient empowerment; Value recognition; Infrastructure and information management; and, ensuring access to care. Ways of overcoming these challenges include: educating healthcare providers, insurance companies, as well as patients on the concepts of personalized medicine. Also, best practices and policies regarding the collection and use of individual information be established. [40]

In the era of next-generation sequencing (NGS) many laboratories, including the Mayo Clinic have launched new molecular and chemical tests as well as new assays for genetic tests. And hopefully, these tests will become more affordable over time. The H3 studies conducted in 4 African countries including Ghana prove that genetic studies can be conducted on a large scale in Ghana including training of experts and capacity building in various aspects of genomics and also showed the benefit of genetic studies in the advent of precision medicine. [42] However, feasibility studies need to be conducted to assess the cost and benefits of conducting genetic studies to look for genes associated with non–adherence in patients with CVD, especially considering the economic impact of CVDs.

Conclusion

Non-communicable diseases, particularly cardiovascular diseases, represent a significant global health challenge, with CVDs being the leading cause of mortality and disability worldwide. Despite advancements in drug therapies, medication non-adherence remains a critical barrier to effective CVD management. However, emerging research in pharmacogenetics and personalized medicine offers promising avenues for improving adherence and treatment outcomes. By integrating genetic, environmental, and lifestyle data, precision medicine has the potential to transform CVD care, offering tailored therapeutic strategies that could significantly reduce the burden of these diseases and enhance patient health outcomes. Continued efforts to explore and apply these advancements are essential for addressing the CVD crisis and achieving better health outcomes on a global scale.

Improving adherence to medication and treatment might be the best investment for tackling chronic conditions such as CVD effectively. And in this era of personalized and precision medicine, why not invest in the genomics of non-adherence?

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CASE REPORTS

RARE INTERNAL HERNIATION OF THE TERMINAL ILEUM INTO A RETROPERITONEAL FOSSA: A CASE REPORT

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Abstract

Introduction: The causes of acute abdomen can riddle many surgeons and clinicians as a whole, amongst which internal hernias are can be illusive puzzles. While clinical history and examination are helpful, they are often nonspecific for internal hernias. The role of imaging can't be overstated in diagnosing the cause of acute abdomen, but we are sometimes welcomed with a completely different picture in theatre than what was diagnosed preoperatively.

Case Presentation: We report a case of a 22year old man, with about a week's history of abdominal pains. Laparotomy revealed a loop of terminal ileum and omentum strangulated in an inferior ileocaecal, retroperitoneal pouch.

Conclusion: The causes of acute abdomen remain to be a mysterious medical phenomenon with a vast array of possibilities. Diagnosing this sometimes comes with difficulty, especially with limited resources. Complete understanding of the aetiology sometimes occurs only at the point of surgical intervention.

Keywords: *hernias, imaging, Laparotomy ileocaeca, retroperitoneal pouch*

Introduction

Internal hernias occur when viscera typically intestine protrudes through a defect such as in the peritoneum or mesentery. This can lead to obstruction and strangulation of the involved bowel. Internal hernias are often difficult to diagnose even with advanced imaging and are often diagnosed intraoperatively.[1,2] This is because the clinical presentations are usually vague and since its rare, it is not often thought of.[1] Additionally, its location masks it during radiological investigations leading to a preoperative misdiagnosis. Herniation into a retroperitoneal recess is even rarer making it a diagnostic challenge. The treatment requires surgery and this possesses a special risk in intraoperatively as these recesses usually have vessels in or near their edges.

Cases Presentation

A 22yr old male, presented with a four-day history of abdominal pain, which started soon after he had some alcohol. He reported to the outpatient department and was managed as gastritis and discharged. However, upon discharge, the patient admitted the pain was still present and persisted till he reported to the emergency department four days after. The pain was described as persistent, diffuse, not specific to any particular region of the abdomen, of varying character, non-radiating, no specific time pattern, with no relieving factors but was triggered and exacerbated by an alcoholic binge. He admitted to multiple bilious vomiting and had not passed stools for the past four days. His past medical, surgical, drug and family history were clinically insignificant.

On examination was a conscious young man in obvious pain. He was afebrile, anicteric, not jaundiced but haemodynamically unstable. His presenting Pulse was 110bpm and blood pressure 108/ 60mmhg. The abdomen was full but not distended, guarded and site of maximum tenderness varied with time (from the epigastric region to the Left lower quadrant). There was no cough impulse at any of the possible external hernia orifices. No palpable masses nor organomegalies but had rebound tenderness and bowels sounds were absent. It was also noted that both testes were retracted to their respective superficial rings and digital rectal examination reveal a packed rectum with non-bloody stools on the exam finger.

An interim diagnosis of acute abdomen was made and resuscitation started immediately. Due to the history of alcohol, we entertained the possible causes were acute pancreatitis or exacerbated peptic ulcer. We also considered hollow viscus perforation, intestinal obstruction and acute appendicitis as differential due to the nonspecific nature of his symptoms.

His erect abdominal x-ray revealed multiple air-fluid levels suggesting bowel obstruction, Fig. 1. The Supine abdominal x-ray showed distended loops of small bowel most prominently seen was jejunum evidenced by complete plicae circulares, Fig. 2. A quick abdominal ultrasound also viewed distended small bowel and no free fluid or collected intraabdominal fluid. With these radiological findings, our suspicion was shifted more towards intestinal obstruction but not sure what the

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mechanism was. An abdominal CT scan may have helped pinpoint the aetiology but was unavailable and would have taken about three hours to transport the patient to and from the nearest centre. Our patient was not stable enough for such a journey and more importantly, we considered the clinical information and

Figure 1: Erect abdominal x-rays, arrows showing multiple air-fluid levels.

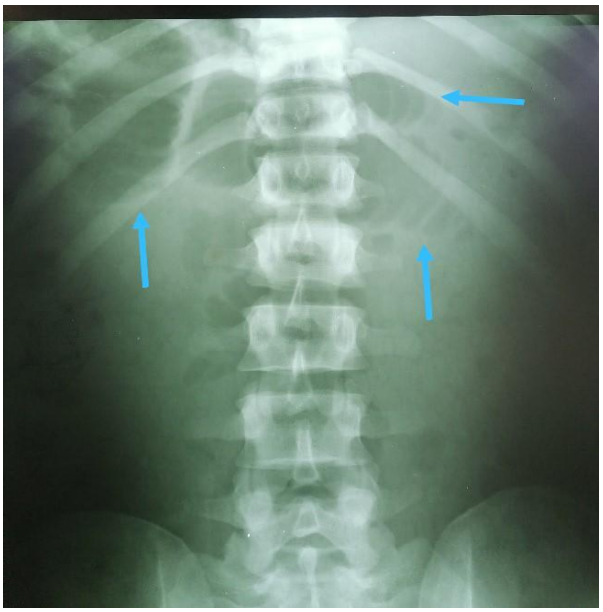

Figure 2: Supine abdominal x-rays, arrows showing dilated jejunum with plicae circulares

available imaging enough to warrant exploration and pursuing further investigations could be termed "diagnostic greed".

Once the patient was adequately resuscitated, he had an emergency exploratory laparotomy. This was done under general anaesthesia and by a midline incision. The intraoperative findings were as follows:

- Grossly distended jejunum and ileum. Seen in Fig. 5
- Terminal ileum and omentum entering a ball-like mass in the retroperitoneal wall at the right iliac fossa. Fig. 3.
- Freed from the structure were gangrenous omentum and about 8cm of terminal ileum with two perforations approximately 4cm proximal to the ileocaecal junction. Fig. 4.
- The contained omentum was about 8cm long, gangrenous and firmly adhered to the base of that structure. Fig. 5.
- A free retroperitoneal pouch once emptied. Fig. 6.

Figure 3: Showing small bowel entering a ball-like retroperitoneal lesion

Figure 4: Showing freed terminal ileum and omentum. Omentum in view.

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The retroperitoneal pouch was partially dissected but not excised to aid in the extraction of its content. A limited right hemicolectomy was performed, gangrenous omentum amputated and the retroperitoneal sac was closed with Nylon 2.0. The abdomen was irrigated thoroughly and closed (fascial) en-masse with

Figure 5: Showing distended loops of small bowel. Green Arrow showing omentum still adhered to the base of the sac

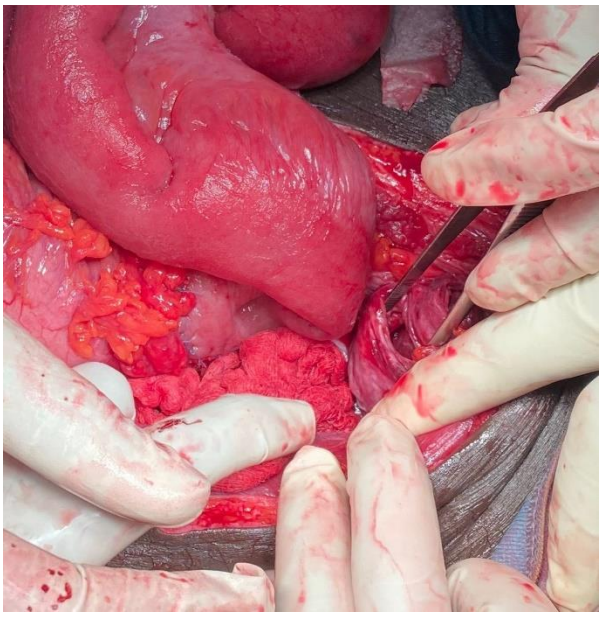

Figure 6: Picture of the now emptied retroperitoneal pouch

interrupted Nylon 2 sutures and skin closed with interrupted Nylon 2.0 sutures.

Post operative (PO) management included, close monitoring, intravenous fluids and analgesics. Intravenous antibiotics were administered for five days and switched to orals since temperature and white cell counts were under control. Deep vein Thrombosis prophylaxis was by way of early mobility and subcutaneous low molecular weight heparin.

On PO Day 3, the patient complained of diarrhoea. It was non-bloody and not associated with any other symptoms. He was managed on intravenous fluids and was already on intravenous antibiotics at the time. His condition had resolved by the following day. The remaining PO period was clinically unremarkable. The patient was discharged on PO Day 11 and reviewed weekly following discharged. He has since resumed his normal activities.

Discussion

Internal hernias constitute 4% of small bowel obstructions and 1% of intestinal obstruction. In this rare cause of intestinal obstruction, viscus, often small bowel loops protrudes into a peritoneal defect.[2,3] These defect occur from defective rotation and fusion of the peritoneum, adhesions, post operative defect or trauma. Thus they can be either congenital or acquired.[1]

The acquired causes are usually following abdominal surgeries, such as stoma formation, small bowel resection and anastomosis, Roux en Y anastomosis, nephrectomies, etc. These involve surgeries that breach the mesentery or retroperitoneal space.[3–5]

Congenital causes of internal herniation are very rare. These can be classified as paraduodenal, intersigmoidal, pericaecal, transmesenteric, transomental, pelvic, supravesical and through the foramen of Winslow. Paraduodenal herniations are classically the most common type of primary internal hernia.[4] They account for 53% of internal hernias and has a male to female ratio of 1:3. It has two subtypes, left paraduodenal hernia where small bowel herniates into the foramen of Landzert and accounts for 75%. The right paraduodenal hernia accounts for 25% of cases, with this, small bowel herniates into the foramen of Waldeyer.[6–8] The broad ligament is a common culprit in pelvic hernias, very rarely there can be hernia through a defect in the pouch of Douglas or distinctively through the an obturator foramen.[4,9,10]

Pericaecal hernia accounts for 13% of all internal hernias. With this, bowel loops, usually an ileal segment herniates into a right paracolic pouch. [6,7] Four types of pericaecal recesses have been described: the superior ileocaecal, inferior ileocaecal, the retrocaecal and the paracolic sulci. Further variations occur due to disparities in individual peritoneal rotation and fusion process or from adhesions.[4]

The clinical presentation is nonspecific thereby leading to diagnostic difficulties. The patient may be asymptomatic and diagnosed incidentally on imaging or laparotomy.[11,12] The symptomatic patient however presents with symptoms of acute intestinal obstruction, such as colicky abdominal pain, vomiting, constipation and abdominal distension. There is usually no obvious mass and the site of tenderness may be imprecise and

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indefinite. Patients presenting late will have features suggestive of complications like obstruction, strangulation and perforation.[1] There have been reports of trapped inflamed appendix in the hernia sac, causing further complications.[13] For pericaecal hernia, patients may present with recurrent colicky pain in the right lower quadrant. The site of this pain may lead to misdiagnosis in favour of an appendiceal disease. High incidence and rapid progression of obstruction and strangulation are seen with pericaecal hernias and the mortality rate can be as high as 75%.[7]

Even though there is evidence that suggest alcohol, tobacco, other dietary habits and diabetes affects collagen metabolism leading to loss of support and structural alterations enhancing the risk of hernia formation,[14,15] this may not be the same pathophysiology our patient. This is because he was not a chronic alcoholic but rather had an alcoholic binge. However, this episode preceding the pain deceptively points towards some non-operable causes of acute abdomen such as acute pancreatitis and peptic ulcer exacerbation. Internal hernias are still to be considered in patient with a history of alcohol intake and acute abdominal pain, especially in those with normal serum amylase.[16]

Even imaging has limited ability in clinching this diagnosis, once again due to its non-specificity. This mostly implies to the utility of ultrasonography and X-rays. Barium studies may be useful but the gold standard imaging modality is the CT scan.[1,6,8] Unfortunately, access to CT scans may prove challenging in many parts of the country. Common CT scan findings include: encapsulation of distended bowel loops within an abnormal location, arrangement or crowding of small bowel loops within a hernial sac, evidence of obstruction with segmental dilatation and stasis, mesenteric vessel abnormalities, i.e. engorgement, crowding, twisting and stretching of mesenteric vessels. [7,8]

Timely surgical intervention based on clinical suspicion or CT scan evidence is warranted for the management of complicated internal hernias.[1] Laparotomy may serve both diagnostic and therapeutic functions. During this, the trapped bowel is released and the distended strangulated bowel can be deflated via needle aspiration and gently reduced.[2] Gangrenous bowel is resected and often anastomosed primarily. Division of the hernia ring is dangerous and ill-advised due to the possible presence of blood vessels in it. The defect is then closed with non-absorbable suture.[1,2]

Conclusions

Internal hernia is a rare cause of acute abdomen but however can be very difficult to diagnose accurately preoperatively. This diagnostic challenge is contributed to by its rarity and the non-specificity of the symptoms. This enigma is made worse when the patient presents with a history of alcohol intake which may point towards other non-operable causes. The astute clinician should have this in mind when diagnosing acute abdomen.

Authors Contribution

EKA had initial contact with the patient, managed the patient, follow-up of the case, conceived and drafted the case report. All authors critically revised the final version of the manuscript.

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Informed Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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THE LAZARUS PHENOMENON: AUTO- CARDIOVERSION AFTER TERMINATION OF RESUSCITATION -A CASE REPORT

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Abstract

Introduction: Lazarus phenomenon is rare, and a dramatic occurrence characterised by a delayed return of spontaneous circulation after cardiopulmonary resuscitation is terminated. We report a case of this rare phenomenon.

Case Presentation: A 45-year-old unemployed man with haemorrhagic pericardial effusion developed iatrogenic perforation of the right ventricle and cardiac tamponade during attempted catheter pericardiocentesis. He became hemodynamically unstable for which he was referred to the cardiothoracic centre and an emergency sternotomy was carried out. He arrested as he was being wheeled to theatre. The sternum was opened, the perforations were repaired, direct cardiac massage was carried out, he was defibrillated 14 times each with 20 joules but there was no response. He was declared dead after 40 minutes of resuscitation. After an additional 20 minutes of no cardiac activity while he was being closed, he regained spontaneous cardiac activity and eventually recovered. Three years of follow up did not reveal any neurological sequelae.

Conclusion: Though the Lazarus phenomenon is rare, it is observable and therefore clinicians should be aware of this phenomenon, and to observe any patient for at least 10-15 minutes (watchful waiting period) using non-invasive monitoring after the termination of Cardiopulmonary resuscitation before confirming death.

Keywords: *Cardiac arrest, auto-resuscitation, Lazarus Phenomenon, spontaneous cardiac activity*

Introduction

Lazarus phenomenon or auto-resuscitation is a very rare occurrence. It is defined as delayed unassisted return of spontaneous circulation (ROSC) following cessation of cardiopulmonary resuscitation which has been deemed unsuccessful and abandoned.

The phenomenon was named after Lazarus of Bethany in the Bible who was resurrected by Jesus four days after his death (John 11:1-45) Linko et al[1] were the first to report this phenomenon in medical literature and the term was first used in 1993 by Bray[2].

Autoresuscitation is uncommon following cardiac trauma, and much more uncommon following open cardiac massage. Our report aims to highlight the peculiar circumstance of this unusual phenomenon occurring following aggressive resuscitation which was terminated with great certainty of clinical death.

Cases Presentation

A 45-year-old male patient was undergoing echocardiography-guided pericardiocentesis via the apical approach for a large pericardial effusion. He became hemodynamically unstable in the middle of the procedure with suspicion of perforation of a cardiac chamber causing cardiac tamponade.

An urgent cardiothoracic surgical consult was sought but suffered cardiac arrest while being wheeled to the operating theatre. Cardiopulmonary resuscitation was initiated and rushed to the theatre, quickly intubated with a hurried skin preparation and draping. A quick median sternotomy was done concurrently with invasive monitoring. Patient had no pulse or ECG activity. Door to sternotomy was conservatively estimated at about 5 - 10 minutes.

The findings were hemopericardium about 1.5L and two puncture points on the anterior aspect of the right ventricle close to the apex which was still squirting. Direct cardiac massage was commenced, and the perforations were repaired with pledgeted sutures. Patient had several episodes of ventricular fibrillation for which he was defibrillated 14 times each with 20 joules. The direct cardiac massage was continued together with boluses of adrenalin and correction of acidosis, transfusion of 2 units of fresh blood with no resumption of spontaneous cardiac activity. We subsequently noticed the heart had become tonically contracted and appeared dusky with no resumption of spontaneous activity after 30 minutes of resuscitation. His pupils were dilated and fixed and was declared clinically dead. Patient was extubated, monitoring discontinued and the family was notified.

We proceeded to close the chest up in layers in the normal fashion, which lasted about 20 minutes in

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preparation for transportation to the morgue. After the closure, a member of the team by stroke of good fortune, checked for a pulse and felt a weak radial pulse following which he raised an alarm. This finding was corroborated by other members of the team, following which monitoring was recommenced, an ECG tracing was now present, and patient remarkably had a sinus rhythm.

He was immediately re-intubated and had an arterial line, central and peripheral lines were re-inserted and full invasive monitoring recommenced. The chest was reopened, right ventricular pacing wires and mediastinal drains were inserted, the chest closed routinely and was sent to the ICU. He developed generalised tonic-clonic seizures on postoperative day 2 and had depressed levels of consciousness with a Glasgow coma scale of 5/15, even though was not sedated the seizures were controlled with phenytoin 100mg 8 hourly and then Keppra 500mg twice daily. He also had Citicoline (somazina) 1000 mg twice daily for obvious hypoxic ischaemic encephalopathy. Tracheostomy was done on the 8th postoperative day on account of prolonged ventilation. He regained full consciousness on the 14th postoperative day and was weaned off mechanical ventilation on 16th postoperative day. He made steady clinical improvement, was fully conscious by the end of the 2nd week with mild cognitive impairments which had resolved as at the time of discharge.

He developed superficial sternal wound infection, which was managed with antibiotics, had tracheostomy decannulated and was subsequently discharged home on the 24th day. On out-patient follow-up over the last 3 years, he has had no gross neurological sequelae but developed osteomyelitis of the sternum (Fig. 2) which was managed successfully with oral clindamycin.

Discussion

Lazarus phenomenon or autoresuscitation was first reported in medical literature in 1982 and the term Lazarus phenomenon was first used by Bray in 1993 [2]. It is probably under reported largely due to medico-legal reasons, fear that people will discredit health professionals and question whether the resuscitation was properly conducted or terminated prematurely [4,8]

Our case was unique in several aspects; Firstly, it followed cardiac trauma albeit iatrogenic. This is quite rare as there is only one previously reported case of autoresuscitation following polytrauma to the best of our literature search [3] · Also, this patient underwent emergency sternotomy with evacuation of 1.5L of clotted hemopericardium ,direct internal cardiac massage, intracardiac injection of 3mg adrenalin and direct defibrillation 14 times with 20 joules each ;Resuscitation was terminated after 40 minutes ;when there was no cardiac activity ,heart has become dusky, all pulses were absent, flat ECG tracing ,pupils were dilated and fixed and patient declared clinically dead with great certainty, extubated and just when skin was been closed for transfer to the morgue he came back to life.

From a recent scooping review by Gordon et al, only about 35% of patients with in-hospital autoresuscitation survive to hospital discharge. Of these subsets, the majority (85%) surprisingly and remarkably have good neurological outcomes [4] .

Our patient did not experience any long-term neurological sequelae after 3 years of follow up.

The Mechanism is not exactly clear [8] ;But multifactorial mechanisms have been proposed to explain this rare occurrence:

(a) Dynamic hyperinflation of the lung causing increased positive end expiratory pressure (PPEP) is one of the proposed mechanisms, which is seen in patients with airway obstructive disease, (b) Myocardial stunning, (c) Delayed action of drugs administered during CPR, (d)transient asystole and (e) hyperkalaemia [1,2].

Our patient showed signs of "resurrection "within the 20 minutes window after termination of cardiopulmonary resuscitation which was consistent with observations made by various authors [4]

The mechanism of autoresuscitation in our patient is still unclear and no single proposed mechanism can explain this scenario [7]; It could be a combination of factors such as Positive end expiratory pressure (PEEP), during CPR dynamic hyperinflation occurs as a result of rapid manual ventilation without time for exhalation, this leads to overventilation and subsequent increased intrathoracic pressure, gas trapping, an increase in the end-expiratory pressure (called auto-PEEP) leading to delayed venous return, low cardiac output and even cardiac arrest. The effect of auto-peep on venous return was also exaggerated by the cardiac tamponade and hypovolemia this patient had. CPR was conducted by an experience team of cardiothoracic surgeons, anaesthesiologists and nurses [5]

Delayed action of drugs used for resuscitation which were administered through peripheral veins were inadequately delivered centrally due to impaired venous return due to the cardiac tamponade and hypovolemic shock; The inotropic drugs therefore did not exert the desired effect on the heart and So after sternotomy, evacuation of the clotted hemopericardium and repair of the ventricular perforation the venous return may have improved coupled with intracardiac injection of adrenaline and atropine [1,2]

The presence of hypovolemia because of right ventricular perforation and hemopericardium may have caused myocardial ischaemia and subsequent myocardial stunning. [1,2]

The implication of this rare phenomenon on our practise as cardiothoracic surgeons has been humbling; firstly, strengthens our faith in the dictum always give your patient the chance in terms of medical care as no cases of autoresuscitation were reported to have occurred without CPR [10]: This patient had coded at the time of our intervention.

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We have learnt to wait for at least 10-15 minutes after termination of CPR before declaration of death indeed patient came to say thank you (Figure 1) to our staff on the day of discharge.

Figure 1: Patient in all white with a sternotomy site dressing came to say thank you to our nurses on the day of discharge from hospital

Figure 2: Sternotomy scar and discharging sinus (blue arrow) from the lower sternal border.

He developed osteomyelitis of the sternum (Figure 2) however the unanswered question is how despite prolonged acute cerebral hypoxia and the poor prognosis associated with autoresuscitation[12], our patient survived miraculously and had no long-term neurological sequelae after 3 years of follow up.

Figure 3: Patient came for last review

Conclusions

Though the Lazarus phenomenon is rare, it is observable and therefore clinicians must be aware of this phenomenon and to observe any patient for at least 10-15 minutes [2,8,9] (watchful waiting period) using non-invasive monitoring after termination of Cardiopulmonary resuscitation before confirming death.

Consent for Publication

Informed consent was obtained from patient and nursing staff before publication of article and use of photos as part of this publication.

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SPONTANEOUS BILATERAL RUPTURE OF THE EXTENSOR TENDONS OF THE KNEE IN PATIENTS WITH CHRONIC KIDNEY DISEASE. CASE REPORTS

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Abstract

Introduction: Bilateral rupture of the extensor tendons of the knee (quadriceps and patella tendons) are uncommon and usually occur as a result of trauma. Spontaneous bilateral tendon ruptures are a rarer injury and has been reported to occur in patients with chronic renal disease and secondary hyperparathyroidism. Patients usually present with sudden inability to actively extend their knee and walk. Over 50% of these injuries are usually missed so a high index of suspicion is required for early diagnosis. These case reports aim to create awareness among physicians and primary care givers about the condition and ensure early diagnosis and management

Case Presentation: We report two cases of spontaneous bilateral knee extensor tendon rupture involving the quadriceps tendon and patella tendon in a 30 year and 50-year-old males respectively. Both patients had chronic renal failure and were on chronic dialysis for a minimum 8 years and were being managed for secondary hyperparathyroidism. One patient had surgical repair and is doing well functionally but the other declined surgery.

Conclusion: Spontaneous knee extensor tendon rupture though rare, occurs in patients on chronic dialysis with secondary hyperparathyroidism. Physicians and primary care givers managing these patients must be aware and maintain a high index of suspicion in order to pick this condition since as seen in our first patient, early treatment is associated with good functional outcomes.

Keywords: *spontaneous, bilateral rupture, extensor tendon, hyperparathyroidism*

Introduction

Simultaneous bilateral quadriceps or patella tendon rupture occurring in patients with chronic renal failure patients undergoing haemodialysis though rare have been reported in the literature.[1–3] There is no consensus on the exact mechanism and pathogenesis, but it is widely believed to be a result of secondary hyperparathyroidism due to repeated dialysis.[1]

Early treatment is associated with better outcomes. We present 2 cases of spontaneous quadriceps and patella tendon ruptures in patients with end-stage renal disease undergoing dialysis. Both had been diagnosed with hyperparathyroidism. One had surgical repair with an excellent outcome but the other one refused surgery. To the best of our knowledge no such case has been reported in Ghana and the West African subregion and these are the first cases from our center.

Cases Presentation

Case no.1

This involves a 30year old male with end stage renal disease who had been on haemodialysis, for the past 10years. He was stable until three weeks prior to presentation when he heard a popping sound in both knees whilst entering the doorway into his house and collapsed onto the floor. He noticed that both knees were swollen, and he could not get up to walk thereafter.

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He was seen and investigated extensively at another facility for a possible spinal injury, a cerebrovascular accident, and possible cardiac issues with negative findings. A diagnosis of his injury was not made, and he was confined to a wheelchair. He was referred to orthopaedic clinic after he complained to the general surgeon managing him for the parathyroid adenoma who after examination thought his inability to walk was most likely from an occult knee injury.

Physical examination showed a young adult male in good health sitting in a wheelchair. Both knees were swollen and tender with a palpable gap between the quadriceps tendon and the patella (Fig. 1). He could not actively extend both knees.

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Figure 1a&b: Swollen left and right knees respectively with palpable gap

A diagnosis of bilateral spontaneous quadriceps tendon rupture was made. The diagnosis was confirmed with an ultrasound scan which showed a complete tear of both quadriceps' tendons at their insertion into the patella. Parathyroid hormone assay was 962.30 pg/ml (normal 16.0-65.0 pg/ml). He was then prepared for surgical repair of both quadriceps' tendons. Intra-operative findings showed the quadriceps tendons were both torn from their insertion into the patella and the tendons had retracted four centimetres (Fig. 2).

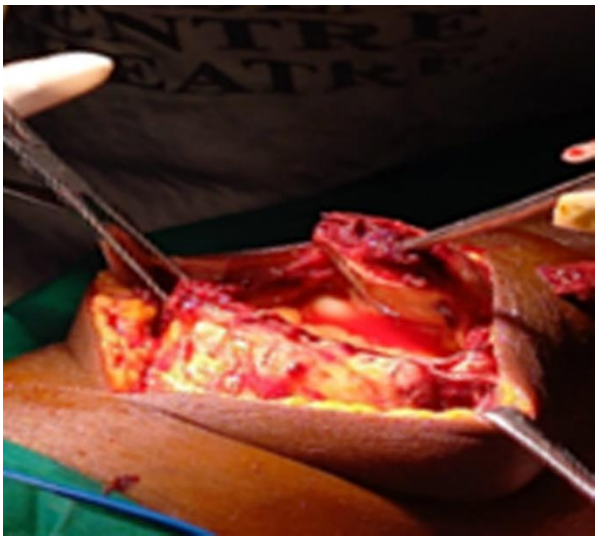

Figure 2: Torn and retracted quadriceps tendon

Under spinal anaesthesia and with the patient in supine position an 8cm longitudinal incision was made over the right quadriceps tendon to the tibial tuberosity. Sharp dissection was done to expose the ruptured quadriceps tendon. Findings were noted and a biopsy taken from the margin of the torn tendon. The quadriceps tendon was repaired by whipstitching of the tendon with a size 5 fibrewire braided non-absorbable suture, tunnelling the sutures through the substance of the patella, and tied over a bony bridge at the distal pole of the patella (Fig 3a-b-c). The integrity of the fixation was tested by flexing the knee, and it was found to be safe to flex to 70 degrees. The wound was then closed, and the same procedure was repeated for the left knee.

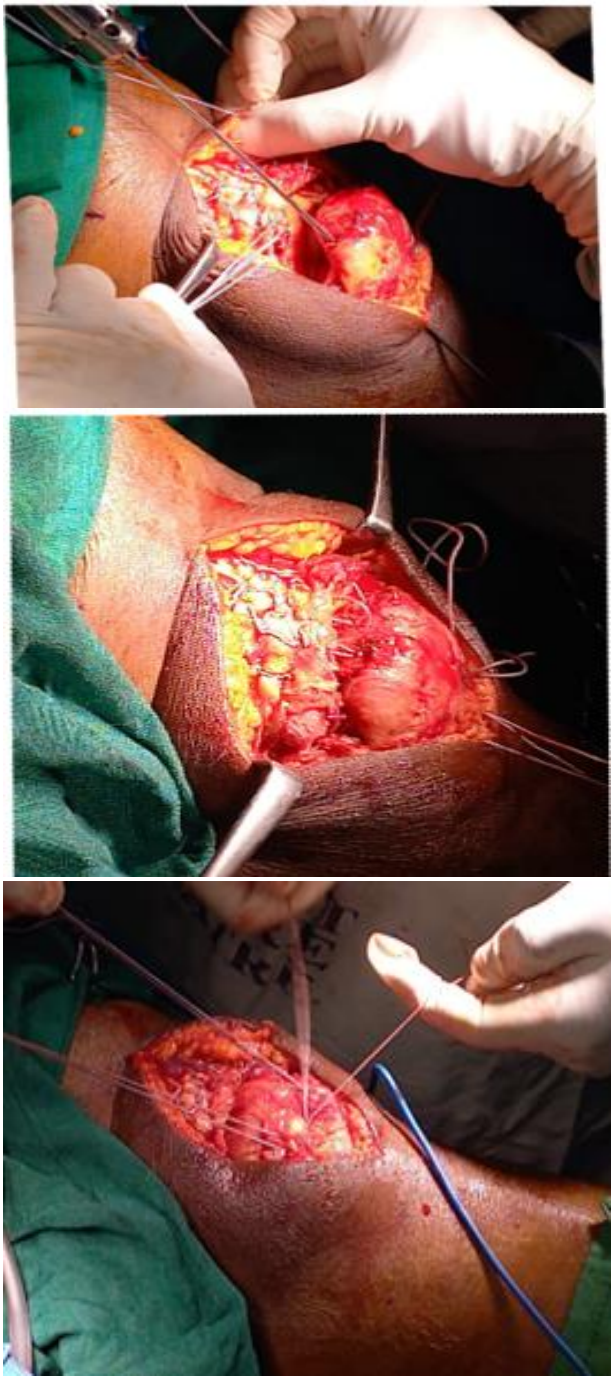

Figure 3: quadriceps tendon whipstitched with sutures (a) and sutures passed through drilled tunnels in the patella (b) and tied over the distal pole of the patella (c)

Post operatively both knees were immobilized in extension with a post-operative brace for two weeks. The knees were examined after two weeks, and wounds seen to have healed after which the skin stitches removed. He was then placed in a hinge brace which was set to 0 to 70 degrees of flexion and was allowed to bear

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weight as tolerable with a Zimmer frame for 8 weeks. He then started muscle strengthening and knee range of motion physiotherapy

Twelve weeks post repair he walked without any aid and the knee range of motion was 0 to 110 degrees on the left and 0 to 100 degrees on the right. He had regained varied strength in the quadriceps and was able to straighten both knees and raise them up to 45 degrees on the right and 90 degrees on the left (Fig 4a-b).

Figure 4-a: right knee extension quadriceps strength

Figure 4-b: left knee extension and quadriceps strength

A biopsy taken from the quadriceps tendon for histopathology was reported as "fragments of fibro-collagenous tissue with areas of haemorrhage and necrosis. There was a cup of reactive round cells in a chondromyxoid matrix with bony trabeculae in areas. There was no evidence of malignancy seen". Histological Diagnosis was reactive/chronic inflammatory changes at the tendon.

Case No. 2

This involved a 50-year-old male with End Stage Renal Disease on haemodialysis for 12 years. Two years prior to presentation, he was descending a flight of stairs when he felt a snapping sound in both knees. He fell down and was unable to walk afterwards. He was seen at a peripheral facility, went through several 'tests' which all came out negative. The diagnosis of bilateral knee tendon injuries was missed, and he was left dependent on a pair of crutches to walk. He had also developed secondary hyperparathyroidism with a parathyroid adenoma and was referred to the General Surgeons who subsequently referred to us on account of a possible knee injury.

On Examination he was unable to walk without aid, his quadriceps muscles were atrophied and unable to extend both knees and raise his legs. The patella was riding high with a gap between the patella and patella tendon on both sides (Fig 5 a-b).

Figure 5-a: 1. Right knee with a palpable gap between the patella and patella tendon

Figure 5-b: Left knee with a palpable gap between the patella and tendon

An ultrasound scan done showed a complete patella tendon tear from its insertion on the distal pole of the patella on both sides. The parathyroid hormone assay done at the time of seeing the patient was 3177pg/ml (normal 16-65pg/ml). He consented to have surgical

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repair of patella tendon after the parathyroid surgery. He however suffered a cardiac arrest intra-operatively during the parathyroid surgery and was successfully resuscitated. He subsequently declined surgery on the knees.

Discussion

The extensor mechanism of the knee comprises the quadriceps muscle and its tendon, the patella, the patella tendon, and the tibial tuberosity. Disruption of this mechanism impairs knee extension hence making standing and walking difficult. Disruption of this mechanism is usually caused by trauma with a patella fracture being the most frequent injury.[1,4] Spontaneous Quadriceps tendon rupture has a low incidence and tends to occur in older people above the age of 50 years.[5] Simultaneous bilateral rupture is even rarer with a reported incidence of less than 5% of all quadriceps ruptures.[6,7] Bilateral quadriceps tendon rupture occurs 5 times more than patella rupture.[8] It usually occurs in patients with chronic systemic conditions such as Systemic lupus erythematosus (SLE), chronic renal disease (CKD), hyperparathyroidism, diabetes mellitus, rheumatoid arthritis and psoriasis.[1,3,9,10] Since Steiner and Palmer reported the first case of simultaneous bilateral quadriceps tendons rupture in a patient with chronic renal failure in 1949, several other cases have been reported.[1,7,10,11]

In a study by Tao et al over an 18-month period, 7 out of 126 patients they saw with Quadriceps or patella tendon rupture had chronic renal failure and were undergoing long term haemodialysis.[8] Two out of these 126 patients had simultaneous bilateral quadriceps or patellar tendons rupture, and both had undergone long term haemodialysis.[8] This makes the incidence of simultaneous bilateral quadriceps or patellar tendon rupture 1.59% (2/126) among patients with quadriceps/patellar tendon rupture. This rate increases to 28.57% (2/7) in patients with chronic kidney disease undergoing long-term haemodialysis.[8]

In a systematic review by Camadaa et al in 2017 which studied 44 patients with bilateral extensor mechanism disruption, 29% were traumatic and 71% were spontaneous with the average age being 53 years.[9] Thirty-seven patients (84%) had bilateral quadriceps Injury, 6 patients (14%) had bilateral patellar injury and 1 patient (2%) had simultaneous quadriceps and contralateral patella injury. Renal disease was found to be the commonest associated medical condition with 61% of the patients having the condition.[9]

Nial Jones et al also reported that 65% of tendon ruptures in chronic haemodialysis patients involve the quadriceps tendon with 11% involving the Achilles tendon and only 8% involving the patella tendon.[12]
The exact pathophysiology is unknown, but most investigators agree that secondary hyperparathyroidism resulting from repeated dialysis plays a major role.[2,11] Other proposed mechanisms include chronic acidosis from renal failure and dialysis related amyloidosis.[12] Histopathology of our first case showed fibro collagenous degeneration with chronic inflammatory changes.

Diagnosis of extensor mechanism rupture is clinical. Up to 50% of bilateral quadriceps rupture may be misdiagnosed[3,5,13] as happened in both of our patients. It is therefore important to have a high index of suspicion in patients with acute knee pain and inability to extend the knee especially in patients with chronic renal failure[7]. For a complete rupture there is palpable gap proximal to the patella. Ultrasound scan was used to confirm the diagnosis of both of our patients. It is quick and cheaper and in experienced hands has a sensitivity and specificity of over 97%.[14] In doubtful cases, an MRI is helpful in making a diagnosis.[1,3] X-rays may be done to rule out fractures and to determine the position of the patella.[3]

Surgical repair is recommended for acute complete quadriceps tendon rupture. This when done within two weeks followed by functional physiotherapy gives excellent results.[4–6,8,15] Our first patient had surgery at 3 weeks post injury and has very good function. The commonest used repair technique is braided non absorbable sutures tied over bony a bridge.[1,16] Suture anchors can also be used.[16]

Post operatively, the knee joint is immobilized for 4-6 weeks in extension after which physiotherapy is done to improve quadriceps strength and range of motion.[3] This has been associated with good function.[3]

Secondary hyperparathyroidism is estimated to occur in about 90% of chronic renal failure by the time they initiate haemodialysis.[1,17] Evidence has shown a strong association between hyperparathyroidism and |spontaneous rupture of the extensor mechanism.[12] Patients on long term haemodialysis usually experience calcium-phosphorus metabolic disturbances which results in secondary hyperparathyroidism[8]. Excessive amounts of parathormone leads to degeneration of tendon tissue.[8] Metabolic acidosis also causes collagen synthesis disorder.[8] Early treatment of hyperparathyroidism reduces the risk of quadriceps and patella tendon ruptures.[12]

Conclusions

We report two cases of spontaneous bilateral knee extensor tendon disruption; one with quadriceps tendon rupture whose diagnosis though missed earlier presented early and had surgery with good outcome. The second case with patella tendon rupture presented late and declined surgery. A high index of suspicion is needed to clinch an early diagnosis and management since it is associated with better outcomes.

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INTRAUTERINE TREATMENT OF FETAL SUPRAVENTRICULAR TACHYCARDIA COMPLICATED BY FETAL HYDROPS: LIVEBIRTH AT TERM

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Abstract

Introduction: Fetal tachycardia is a rare complication during pregnancy, with supraventricular tachycardia (SVT) being a common cause of a primary sustained fetal tachyarrhythmia. If developed early in pregnancy, it can lead to non-immune fetal hydrops (FH). Multidisciplinary approach is mandatory between pediatric cardiologists (both paediatric and adult), neonatologist, and maternal-fetal medicine specialist.

Case Presentation: We present a case of fetal SVT, complicated with FH at 24 weeks' gestation, which was successfully treated with transplacental flecainide to emphasize the need for prenatal evaluation of pregnancies complicated by FH and provision of appropriate treatment to optimize outcome. 35-year-old MPLK; with a gravidity of 1 and parity 0, was referred to our Fetal Medicine Clinic due to an increased fetal heart rate (FHR) of 243 beats per minute during a routine fetal anatomical survey scan at 22 weeks gestational age (GA). The pregnant woman and the fetus had no clinical symptoms, and clinical examinations and investigations revealed no organic lesions. The fetus developed congestive heart failure evidenced by cardiomegaly, pericardial effusion, ascites, and skin edema at 24 weeks' gestation. The couple made an informed decision for transplacental antiarrhythmic therapy which resulted in successful fetal cardioversion, with minimal maternal side effects. Delivery was conducted at 37W GA, and baby is currently 4 months old and well.

Conclusion: Prenatal evaluation of pregnancies complicated by fetal hydrops is necessary to determine the underlying etiology and provide appropriate treatment to optimize outcome.

Keywords: *fetal tachycardia, supraventricular tachycardia, fetal hydrops, echocardiography, cardioversion*

Introduction

Fetal tachycardia (FHR ≥180 bpm) affects 1% of pregnancies, with sustained tachyarrhythmias occurring in 0.1%[1]. Supraventricular tachycardia (SVT) is the most common type[2], and if untreated, can lead to fetal hydrops (FH) and intrauterine death. Diagnosis relies on Doppler ultrasound in resource-limited settings, and management includes monitoring, transplacental therapy, or preterm delivery. This case is unique due to the early diagnosis of SVT with FH at 24 weeks' gestation and its successful resolution with transplacental flecainide, demonstrating the potential for early intervention even in low-resource settings.

Cases Presentation

A 35-year-old primigravida was referred at 22 weeks' gestation due to fetal tachycardia (FHR: 243 bpm) detected on routine ultrasound. She had no systemic illness, infections, or thyroid dysfunction, and all antenatal labs were normal. Fetal echocardiography confirmed a structurally normal heart with persistent SVT (1:1 atrioventricular conduction) [Fig.1]. At 24 weeks, the tachycardia persisted (244 bpm) with evolving hydrops fetalis (cardiomegaly, pericardial effusion, ascites, and skin edema), leading to a definitive diagnosis of fetal SVT complicated by hydrops [Fig.2a,b]. Maternal transplacental therapy was initiated with oral digoxin, but fetal tachycardia persisted. At 25 weeks, flecainide was added, resulting in a gradual reduction of FHR to 140–160 bpm by 27–31 weeks [Fig.3], with resolution of hydrops [Fig.2c]. At 32 weeks, the mother developed transient headaches and blurred vision, prompting a reduction in flecainide dosage. At 37 weeks, she underwent an elective cesarean section, delivering a healthy male baby (2.6 kg, APGAR 8/9) with a stable heart rate of 120 bpm. The neonate required no antiarrhythmic therapy and was discharged after brief NICU monitoring. At five months, the infant was thriving with normal growth and development. Parents were counseled on potential SVT recurrence and advised on long-term pediatric cardiology follow-up.

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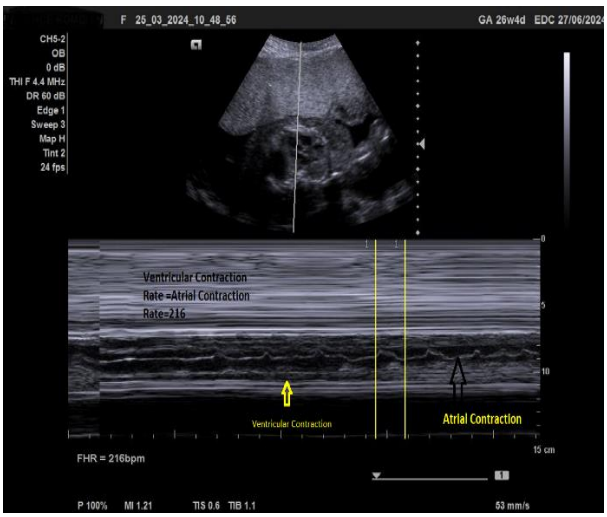

Figure 1: Fetal Tachyarrythmia

Figure 2a: Thermal Images at (2a) 26 weeks 4 days showing regression of fetal ascites

Figure 2b: Thermal Images 29 weeks days 1 day showing regression of fetal ascites

Figure 2c: 33 weeks 0 days showing regression of fetal ascites

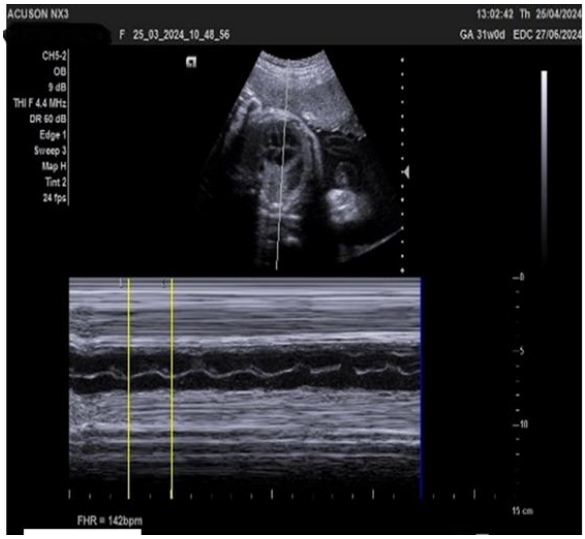

Figure 3: Thermal images showing fetal heart rates at 31 weeks

Discussion

Fetal supraventricular tachycardia (SVT) is typically an isolated finding, with structural heart abnormalities present in up to 11% of cases.[3,4] In this case, detailed fetal echocardiography ruled out structural defects, negating the need for invasive genetic testing. The predominant cause of fetal SVT is atrioventricular reentrant tachycardia (AVRT), which was strongly suspected based on echocardiographic findings, though pulsed-wave Doppler (PWD) could have further confirmed the diagnosis. Sustained fetal tachyarrhythmia exceeding 200 bpm increases the risk of fetal heart failure and hydrops, with hydrops significantly worsening prognosis.[5,6] Early onset (<32 weeks) and persistent tachyarrhythmia further elevate this risk, necessitating prompt treatment.[5,7,8] Given the progression to hydrops at 24 weeks, transplacental therapy was initiated to prevent adverse outcomes.

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Digoxin is commonly the first-line treatment for fetal SVT, but its efficacy diminishes in hydropic fetuses.[9] Flecainide has demonstrated superior bioavailability and arrhythmia control, especially in hydropic conditions.[10-13] This case supports literature findings, as digoxin failed to resolve the tachycardia, but flecainide successfully restored sinus rhythm and reversed hydrops. Maternal tolerance to antiarrhythmics can impact treatment success. Despite comprehensive pre-treatment screening, the patient developed transient symptoms suggestive of drug intolerance at 32 weeks, necessitating dose adjustment. While maternal mirror syndrome and preeclampsia were considered, targeted evaluations ruled them out. Delivery timing remains variable, though most centers aim for 38 weeks. In this case, cesarean delivery at 37 weeks was chosen due to the absence of serum flecainide monitoring. Postnatal follow-up is crucial, as prolonged fetal arrhythmias and hydrops may affect neurodevelopment. This case highlights the effectiveness of transplacental flecainide therapy in fetal SVT with hydrops, aligning with existing evidence on its superiority in refractory cases.

Conclusions

Early detection and intervention are crucial in managing fetal SVT, particularly when complicated by hydrops. This case demonstrates the effectiveness of transplacental flecainide therapy in achieving successful cardioversion, especially when first-line digoxin therapy fails. Careful maternal monitoring and dose adjustments are essential, especially in low-resource setting with no capacity for maternal serum flecainide monitoring. The case also reinforces the importance of prenatal evaluation, individualized management, and postnatal follow-up to optimize pregnancies complicated with fetal SVT in low-resource setting.

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ACKNOWLEDGEMENT OF REVIEWERS

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FROM THE PAST

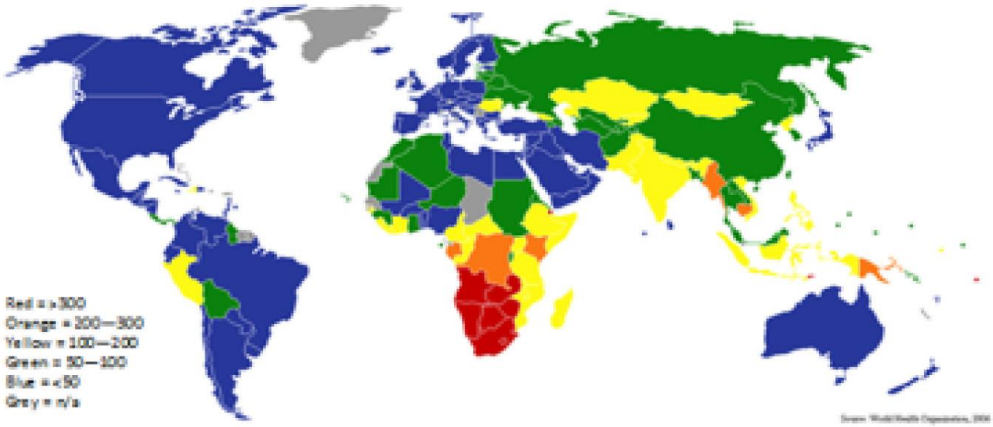
RURAL HEALTH:
FROM DISEASE ERADICATION TO MEDICAL FIELD UNITS

During the 1930`s, reported rates of trypanosomiasis (Sleeping sickness) and yaws increased. Along with malaria, yaws was considered to be one of the biggest contributors to ill health in the country, with the heaviest burden in the north but a significant burden everywhere. In Accra, Cape Coast, Sekondi and Kumasi, 30% of children reporting to infant welfare centres had yaws. In 1937,the government undertook a trypanosomiasis control programme and 1944 a yaws eradication campaign was launched. Both campaigns where enormously successful in reducing the incidence of disease.

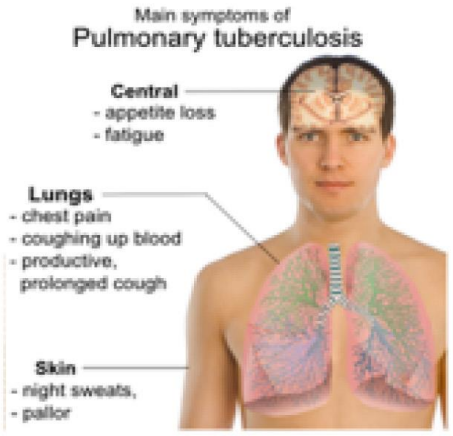
Governor Burns advocated for the continuation of medical services to rural areas as the eradication campaigns reached an end. He assigned personnel from the eradication campaigns to medical field units and arranged for them to receive additional training in the identification of several common diseases and pathogens in rural areas (such as malaria, guinea worm, bilharzias, leprosy) as well as training in basic vaccination and laboratory work. Headquarters was at Kintampo, centrally located for rural outreach work. Drs. Waddy and Saunders provided the leadership for the organization and development of the Medical Field Units.

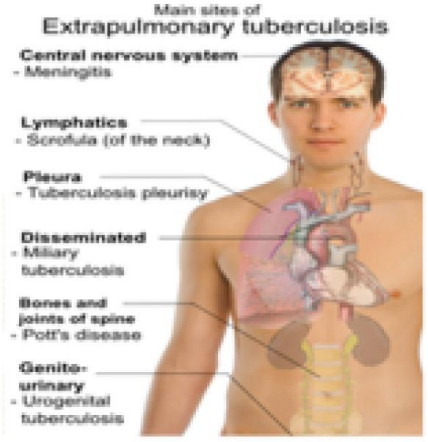
Doctors such as Dr. Akiwumi, M.A. Barnor, and Frank Grant undertook groundbreaking medical research based out of the Medical Field Units, including the gathering of data on bilharzias, onchocerciasis, and guinea worm.

TUBERCULOSIS



World map showing reported cases of tuberculosis per 100,000 citizens. Red = >300, orange = 200—300, yellow = 100—200, green = 50—100, blue = <50 and grey = n/a





Tuberculosis (TB) is a disease caused by a small bacterium called Mycobacterium tuberculosis. The most common form of the disease is when it damages the lungs, but it can affect many parts of the body, when it is called extra-pulmonary disease. TB is highly infectious and is usually caught by breathing in bacteria from the air. People with untreated disease in their lungs or throat expel the bacteria as small droplets when they cough, sneeze or even during talking. These tiny droplets can remain suspended in the air for long enough to be inhaled by other people in the vicinity.

When the disease becomes active, 75% of the cases are pulmonary TB. In the other 25% of active cases, the infection moves from the lungs, causing other kinds of TB, collectively denoted extra-pulmonary tuberculosis.

People with damaged immune systems have a much higher risk of developing TB disease. TB is the leading cause of illness and death in people living with HIV. HIV/AIDS and TB are so closely connected that the term "co-epidemic" or "dual-epidemic" is often used to describe their relationship.

Treatment for TB uses antibiotics to kill the bacteria. The two drugs most commonly used are rifampicin and isoniazid. However, instead of the short course of antibiotics typically used to cure other bacterial infections, TB requires much longer periods of treatment (around 6 to 12 months) to entirely eliminate mycobacteria from the body.

PMJG Editorial Policy

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Book Chapter

Philips SJ, Whisnan JP. Hypertension and stroke. In: Laragh JH, Bremner BM, editors, Hypertension: pathophysiology, diagnosis and management. 2nd Ed. New York: Raven Press, 1995, p465-478.

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