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AIMS & SCOPE

HMDJ is the journal of HITEC Institute of Medical Sciences (HITEC-IMS), Taxila. It is an open access, peer-reviewed, bi-annual journal that aims to keep the medical & dental health professionals updated with the latest information relevant to their fields.

HMDJ welcomes scholarly work from medical, dental and allied subjects (basic & clinical), community health issues and medical education. It publishes original research, review articles, case reports, editorials, letters to editor, short communication, book reviews, recent advances, new techniques, debates, adverse drug reports, current practices, and conference reports. All publications of HMDJ are peer reviewed by subject specialists from Pakistan and abroad.

OBJECTIVES

1. To publish original, peer reviewed clinical and basic sciences articles.
2. To promote research culture in HITEC-IMS and beyond, by inculcating the habit of medical writing in doctors.
3. To assist physicians to stay informed about the developments in their own & related fields.
4. To support knowledge & experience sharing among the health professionals for the benefit of the patients.
5. To attain top-notch ethical medical journalism by delivering credible and reader-friendly publications.

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MEDICAL ETHICS: READY TO SEE THE MIRROR?

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Our world is faced with an existential crisis. As we make substantial strides in technology, innovation, and production, we also witness heartbreaking deprivation, disease, and death. There is an ever-growing divide between those with abundant resources (far exceeding their needs) and those with minimal to none. Disparities, including those in healthcare, have become stark and undeniable. These disparities exist across multiple dimensions and include disparities in access to care, patient outcomes, and what is valued by healthcare systems versus what is valued by physicians. The common denominator driving these disparities seems to be privilege. Privilege, defined as "a special right, advantage, or immunity granted or available only to a particular person or group", is often tied to financial status. Just like high-income countries can get away with massacres, wealthy individuals can evade legal repercussions of unlawful acts. The global stage and societal institutions hence reward and reinforce the acquisition of resources and privilege above anything. This leads to greed. Greed has also found its way into our profession (Medicine). Dr. Sania Nishtar's book is a massive indictment. It tells us about corruption and the endemic injustices in Pakistan. They are like choked pipes of Pakistan's health system. They deny Pakistanis their rights to health and health care[1]. We risk losing our identity as healers and becoming mere employees and beneficiaries of the healthcare industrial complex. This editorial is an attempt to remind ourselves of the oaths we took. I have worked as a physician for 45 years and over these four and a half decades, I have seen the changes in the moral campus of our healthcare sector. Doctors have become businessmen, and the health sector has become the health industry. Private hospitals and private medical colleges are now open to mint money. Medicine is no longer a noble profession. The people are also more demanding now and they want the doctors to work like the professionals abroad. This is due to awareness through print and social media[2]. I will use the four pillars of medical ethics to highlight where and how we violate our oath and what can be done.

CAPSULE SUMMARY

The health sector has evolved into an industry and physicians have turned into entrepreneurs. Private medical colleges and hospitals are minting money. People are also more aware now and they expect doctors to work like professionals abroad. The basic pillars of medical ethics like patient consent, Justice, confidentiality, beneficence and non-maleficence must never be compromised. The unholy nexus of doctors with pharmaceutical companies, laboratories and imaging facilities should be discouraged. Students should be taught medical ethics right from the beginning. Unethical research practices must be stopped.

Autonomy

Physicians should always use a collaborative and patient-centered approach. A hierarchal approach in which the physician tells a patient what to do, without fully explaining the diagnosis, treatment choices, risks, benefits, & alternatives, violates the principle of autonomy. The patient has to live with the side effects of the treatments that we propose, and therefore, it is imperative that they know the side effects and freely consent to the treatment. Unfortunately, some physicians in Pakistan do not share the diagnosis and rationale for treatment with their patients. The alternatives and side effects are hardly discussed. Even consent for major procedures such as surgeries is obtained in a rushed and coercive manner and by personnel not qualified for it. Residents sometimes perform surgeries without supervision and proper patient consent, even in the teaching hospitals[3].

Justice

The remnants of colonisation and the stratification of people, based on their socio-economic status and accumulated privilege can be seen within the healthcare sector as well. The patients are categorised as very, very important person (VVIP), very important person (VIP) , and those admitted to general wards. The way physicians approach these patients and their level of empathy and compassion is also contingent on their categorisation. A VVIP patient will receive superior care than other patients. Patients who visit government hospitals and are admitted to general wards sometimes have to wait for hours, are denied adequate care because of a lack of resources, are not adequately heard and examined due to high patient loads, and are dismissed and sent away due to an over-extended physician

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workforce. A patient who was never properly assessed, was never told his diagnosis, and has no means to secure treatment will have suboptimal outcomes. Dr. Martin Luther King said, "Injustice in health is the most inhuman form of inequality because it often results in physical death". Moreover, the healthcare budget remains abysmal (0.04% of the Budget), and whatever is allocated is unsafe because of corrupt practices[4].

Confidentiality

Patient confidentiality is paramount. A patient puts his/her trust in their physician, and this trust is an honour and privilege for physicians. However, trust is violated when a patient is assessed and examined by others in the same room who can overhear the conversation between the patient and their physician. Lack of resources should not deter physicians from ensuring adequate patient privacy and confidentiality. Also, a physician is barred from sharing patient information with anyone, without proper release of information documents, which the patient must voluntarily consent to. Therefore, any communication about the patient, with others, is unethical. However, confidentiality is not absolute. This principle can be breached in certain situations and must be breached in other situations[5].

Beneficence and non-maleficence

The central principle of Medicine is patient care, beneficence. Everything we do, should be in service of the benefit of the patient. It saddens me to share that I have seen this principle undermined. Sometimes, physicians' convenience and availability, financial responsibilities towards themselves or the institutions they work for, relationship with pharmaceuticals, etc., take precedence. Non-maleficence means "do no harm". This is the least physicians can do for their patients, to not harm them volitionally. Unnecessary investigations and polypharmacy (including prescription of food supplements and nutrients without evidence-based benefits) put patients at risk. Polypharmacy risks the patient not only due to side effects but also because of the possible drug interactions, which sometimes physicians do not take into account. Another way we can harm our patients is by charging them exuberant sums of money. Yes, physicians are entitled to compensation for their expertise, but it's also imperative to be just and measured . We are a low-income country, where many patients cannot afford our services / recommended treatment. Therefore, we must be careful and prudent in discerning which investigations, procedures, and medications are absolutely required. Alliances and relationships with pharmaceutical companies and laboratories are obvious conflicts of interest.

Unholy nexus of doctors (health industry) and pharmaceutical representatives (pharmaceutical industry)

The ethos of a society is intricately linked with the character of its people, their values, and the role that tradition and religion play in their lives. Thus, medical ethics differ in some aspects, in the developed and the developing countries. The fear that financial motivation may lead to unethical practices by individual physicians results from changing medical practices and a failing national economy. Remuneration by pharmaceutical agencies, increasing user fees, burgeoning private practices, and the increasing use of diagnostic technologies add to the changing financial landscape. An overall scarcity of resources in Pakistan makes these changes more acute and visible, especially as public access and quality of care still have much to be desired. Unfortunately, there is an unholy nexus between doctors and pharmaceutical representatives at the individual and higher levels. The pharmaceutical companies, through their representatives, bribe the doctors with cash, costly gifts, and so-called educational and recreational trips within Pakistan and abroad where they stay in five-star hotels, food is paid, and their trips to recreation places are planned. In return, they would indiscreetly write their medicines, food supplements, and multivitamins. They also choose doctors to do fake research for their products and share this with the healthcare providers and patients. There is a mushrooming of pharmaceutical companies, and the efficacy of their medicines is not rightly assessed. Many clinical setups have their own pharmacies, with medicines available exclusively there. Thus, patients must return to the same doctor to purchase the medication. Only a minority of doctors preserve their honesty and integrity. As Jung (2002) writes, "Once you have sold your soul, it can be a hard item to retrieve". [6,7,8]

Pathological relationship between doctors and laboratories/imaging facilities

Doctors are given incentives and cuts in writing tests from a particular laboratory or imaging facility. Many doctors have their own laboratory or imaging, thus writing unnecessary investigations.

Ethical issues in research

Due to high patient volumes in Pakistan, research can take a backseat. Without allocating protected time and resources, the study quality becomes subpar. Even scholarly work, such as writing and publishing articles, is fraught with unethical practices. The research articles are mandatory for promotion, but the institutes do not provide protected time and resources. This has led to a new business, fake article writing. The research tasks are delegated to junior physicians and postgraduate residents at the teaching institutes but their contribution is not acknowledged as first authors. Senior physicians, without contribution to the manuscript, are included and prioritised in authorship. Sometimes, in haste, the manuscripts are plagiarized, and the quality of work is sub-optimal. Research is conducted without paying heed to ethical considerations. Peer reviews are of low quality, and the journals publish anything provided the physician is willing to pay. In this context, the quality of scholarly and research work becomes questionable and raises doubts about it being truly evidence-based. Therefore, with global partnerships in research, Pakistan has to change this culture[9].

Teaching medical ethics

As physicians, most of us consider ourselves ethical and self-righteous. We rationalise our corrupt practices by believing that private practice is a contract between the consultant and the patient governed by personal ethics. The consultants and

teachers are the role model for many. There is no such thing as "personal ethics". There are ethical principles and codes of conduct, by the regulatory bodies. The ethical and moral principles, embodied in the code of conduct for doctors, clarify the patient's rights and the doctor's responsibilities. However, these principles are not known, understood, or practised[10]. Students learn by observing us. Although in the past, medical ethics were not that explicitly taught, they were practised by the supervisors and the mentors. Now, they are taught in the classes, but their practice is diminishing. Students can memorize these terms, and we can quiz them. However, without proper role modelling, we cannot expect them to adopt these principles in their practice. Senior physicians, supervisors, and mentors must role-model ethical behaviours towards their students. We are being watched, our conduct influences younger physicians, and we are responsible for them and their future patients. This is my plea to call all my colleagues to uphold medical ethics. The future of our profession depends on our current behaviours.

CONCLUSION

I request my colleagues to read this editorial with self-reflection. Do not be dissuaded by its focus. We have to confront the malpractices that have become rampant in our field. When you incise an abscess, the pus comes out for a while; however, the actual healing occurs after that. I wish that our profession heals its soul.

I recommend that my colleagues read and act on the Code of Conduct by the Pakistan Medical and Dental Council(PMDC). This code needs to be revised every five years, given the advancements in medical sciences, have led to new ethical dilemmas.

The specialties and sub-specialties should also make a code of conduct, encompassing their specific issues, like the Madrid Declaration on Ethical Standards for Psychiatric Practice Approved by the General Assembly of the World Psychiatric Association in Madrid, Spain, on August 25, 1996, and enhanced by the WPA General Assemblies in Hamburg, Germany on August 8, 1999, in Yokohama, Japan, on August 26, 2002, and in Cairo, Egypt, on September 12, 2005. Other specialities can make similar codes of ethics.

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ORIGINAL ARTICLE

ROLE OF ASEPTIC MEASURES IN PREVENTING SURGICAL SITE INFECTIONS IN SKIN BIOPSY PROCEDURES

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ABSTRACT

Objective: To evaluate the role of aseptic measures in preventing surgical site infections in skin biopsy procedures.

Study design: Prospective, observational study.

Place and duration of study: Department of Dermatology, PAF Hospital, PAF Base Faisal, Karachi, 16 months (October 2019 to January 2021).

Methodology: The study included all patients who underwent skin biopsies, except punch and shave biopsies during the study period. The procedure was done under strict aseptic measures in a dedicated room of the operation theatre, according to the standard protocol, and the patients were followed up for any surgical site infection. Demographic data of the patients along with other parameters, including comorbid conditions, presence or absence of surgical site infection, site of biopsy, type of biopsy, and type of sutures applied were recorded for each patient by direct observation. Data were analyzed using SPSS version 18.

Results: Total 151 patients, with a mean age of 36 ± 14 years, were included in the study. Out of 151 patients, 99 (65.6%) were males and 52 (34.4%) were females. Excision biopsy was done in 58 (38.4%) and incision biopsy in 93 (61.6%) patients. The most commonly biopsied site was the trunk (45 patients). Wound infection was present in 04 patients. Out of the 04 infected patients, 02 had diabetes mellitus and 01 was a smoker.

Conclusion: Effective aseptic measures reduce surgical site infections in skin biopsy procedures.

Keywords: *Biopsy, Dermatology, Surgical wound infections.*

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INTRODUCTION

Skin is the largest organ of the body accounting for 15% of the total body weight [1] . It comprises a unique and complex structure and has varied and extremely diverse functions [2] . It not only acts as a mechanical barrier against external harmful agents but also functions as an immunologic organ and helps in maintaining body temperature and electrolyte balance, in addition to numerous other functions [3].

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Considering the composite structure and diversified functions of the skin, this organ hosts a spectrum of diseases, ranging from primary inflammatory and immunologic disorders to neoplastic lesions and secondary involvement of systemic disorders [4,5]. Proper and thorough physical examination is the corner stone for reaching a correct diagnosis of skin diseases [6]. Clinical examination alone is not helpful in reaching the accurate diagnosis in most cases and the maximum a dermatologist can achieve, is a list of differential diagnosis, narrowing the broad spectrum of skin diseases [7]. In these circumstances, skin biopsy becomes the primary diagnostic modality for a definite diagnosis [8].

Skin biopsy is a relatively simple procedure which is done under local anesthesia as an outpatient department procedure [9]. If proper care and antiseptic measures are taken, this procedure is uneventful. However, complications arise in some cases, surgical site infections (SSI) being the most common [10]. Other

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complications include pain, bleeding, dehiscence etc. There are many factors which can lead to complications such as humid environment, improper sterilization, site and type of biopsy, use of steroids, comorbid conditions such as diabetes mellitus and biopsy setup [11].

Prophylactic antibiotics are generally used to prevent wound infection in skin biopsies. Their use in clean wounds is usually less warranted, however, it is recommended in certain conditions such as dirty wounds [12]. Factors such as immunosuppression and humid environment also favor the use of antibiotics [13].

CAPSULE SUMMARY

Strict aseptic protocols during skin biopsy operations can significantly reduce wound infections, eliminating the need for topical or oral antibiotics. Antibiotic resistance will ultimately decline if unneeded antibiotics are avoided during minor surgical procedures like dermatological surgery.

Although antibiotic use can help prevent wound infections, it has a few drawbacks as well, one of the most important being, antibiotic resistance[14,15]. One of the measures to decrease the risk of post-skin biopsy wound infections without using antibiotics is to follow strict aseptic measures, performing the procedure in a dedicated operating room as an additional aseptic measure[16]. A thorough search of the electronic media revealed that no study has been conducted in Pakistan to evaluate the impact of aseptic measures in dermatologic biopsy procedures to prevent surgical site infections.

This study was thus designed to assess the effects of aseptic measures in preventing wound infections in skin biopsy procedures in a military hospital in Karachi. These measures can lead to decreased use of antibiotics and ultimately result in a decline in antibiotic resistance.

METHODOLOGY

This prospective, observational study was done in the Department of Dermatology, PAF Hospital, PAF Base Faisal, Karachi, from 23 October 2019 to 15 January 2021. The sample size of 151 was found with the World Health Organization (WHO) calculator, with a confidence interval of 95% and a margin of error of 5%. All patients reporting to the out-patient section of the Dermatology department, with skin lesions underwent either incision biopsy or excision biopsy, for diagnostic or therapeutic purposes, were included in the study by a non-probability convenience sampling technique. Informed consent of the patients and approval from the hospital's ethics committee (Reference number: IRB/Faisal/06/2019, Date: 6-6-2019) were obtained. Patients unwilling to undergo biopsy, patients requiring punch or shave biopsies, patients having infected wounds/ lesions or bleeding tendencies and those on anticoagulant therapy were not included in the study.

The steps of the procedure were explained to the willing patients. A brief clinical history was taken and any comorbid conditions, such as smoking or diabetes mellitus, were recorded. The procedure was done in a designated room of the operation theatre under strict sterilization. Sterile, packed and non-reusable gloves were worn by all individuals involved in the procedure. The biopsy site was scrubbed with Pyodine, as per protocol. For maximum effect of Pyodine ,05 minutes were given. A local anaesthetic agent (1% lignocaine with adrenaline) was used. A surgical towel was draped to maintain the sterilization field. Biopsy was performed depending on the nature of the lesion. Incision biopsy was mainly done for diagnostic purposes, and excision biopsy for both diagnostic and therapeutic purposes. Therapeutic excision biopsies were taken from pilar and epidermoid cysts of the face, trunk and axilla. Excision biopsies were done in suspected patients of basal cell carcinoma, actinic keratosis with atypical symptoms, Bowen's disease, glomus tumour, pyogenic granuloma and other neoplastic lesions of the skin. After biopsy, the wound was stitched with appropriately sized interrupted proline sutures. Where larger sections of the skin were taken, mattress sutures were applied. Excision biopsies of the face were closed using subcuticular sutures for maximum cosmetic effect. For nail bed and oral mucosal biopsies, absorbable chromic sutures were used instead of proline sutures. Following biopsy, the surgical site was scrubbed with Pyodine to cater for any residual blood which is a source of infection as it acts as a substrate for bacterial growth. A simple dressing with Polymyxin was applied on the stitched wounds other than those of oral mucosa. Patients were asked to come to the department for a dressing change the next day. They were also instructed about wound care like, keeping it dry & away from dust and unnecessary exposure. Stitches were removed after five days for facial biopsies and seven days for the rest of the body sites. The biopsy site was observed for wound dehiscence and any signs of infection including erythema, pain, swelling, and pus discharge. If the biopsy site was infected, a five-day course of oral Co-amoxiclav 626 mg thrice daily along with topical Fucidic acid was prescribed and the patients were instructed to come for follow-up after five days.

Demographic data including name, age and gender of all patients were recorded along with other parameters such as site, size and type of biopsy (Incisional or excisional), type of sutures applied (Interrupted, mattress or subcuticular), comorbid conditions (Diabetes Mellitus, smoking, none), days after which the stitches were removed (05 days, 07 days or absorbable sutures), wound dehiscence and wound infections (present or absent). Data were recorded on a proforma, based on direct observation.

The data were analyzed, using SPSS version 18. The means and standard deviation were calculated for the numerical variables, like age. Frequencies & percentages were presented for the categorical variables for example gender, site and type of biopsy, type of sutures applied, comorbid conditions, days after which the stitches were removed, wound dehiscence and SSI.

RESULTS

The study was conducted on total of 151 individuals. The mean age of the patients was 36 ± 14 years with the minimum and maximum ages of 5 and 83 years respectively. Out of 151 patients, 99 (65.6%) were males and 52 (34.4%) were females.

Excision biopsy was done in 58 (38.4%) patients and incision biopsy was done in 93 (61.6%). The most common site biopsied was the trunk i.e., in 45 patients. The frequency of skin biopsies done from various sites of the body is summarized in Table 1. The mean size of the skin biopsy was 8 ± 1.2 mm with a minimum size of 4 mm to a maximum of 20 mm. After the skin biopsy, interrupted sutures were applied in 101 (66.9%) cases, subcuticular sutures in 36 (23.8%) and mattress sutures in 14 (9.3%) cases. Number of patients having comorbid conditions is summarized in Figure 1. Based on the site of the biopsy, the sutures were removed after either 05 days or 07 days, its frequency is compiled in Figure 2. Total 04 patients (2.6%) patients developed SSI (Secondary bacterial infection of surgical wounds) and the remaining 147 (97.4%) patients showed no complication in the skin biopsy wound. Total 03 infected wounds were from the leg and 01 from the trunk. The frequency of wound infection in comorbid conditions of the patients is summed in Table 2.

None of the biopsy sites showed wound dehiscence. In the infected wounds, the need to remove stitches prematurely was not mandated, as the infection in all the cases settled after 05 days of oral antibiotics.

DISCUSSION

Skin biopsy is the main diagnostic tool available to dermatologists. Its diagnostic importance cannot be over-emphasized in dermatology practice. The current dilemma of rising antibiotic resistance has highlighted the need to redefine the need for the prescription of antibiotics. To reduce the incidence of SSI, surgical antibiotic prophylaxis (SAP) is an evidence-based practice [17]. Antibiotic prophylaxis in dermatological surgery is recommended in special circumstances such as prosthetic heart valves or joints. World Health Organization has defined antibiotic resistance as the biggest threat to global health [18]. The commonly prescribed topical antibiotics include bacitracin, polypore, mupirocin, hydrogen peroxide and non-antibiotic ointments including petrolatum-based products [19]. These are employed in pre and post-procedure wound care. Antiseptics are also advised to reduce SSI. Overzealous use of topical antibiotics to guard against infection has contributed to enhanced bacterial resistance and is currently not recommended, in clean wounds, by the American Academy of Dermatology [20,21] .

The risk of SSI depends on comorbid conditions and the environment. The patient-related comorbidities include advanced age, diabetes mellitus, renal disease, immunosuppression, smoking, obesity etc. Environmental factors include length and technique of the procedure, preoperative sterilization and aseptic measures [22] .

Bacteria can gain entry into the wound if sterilization protocols are improperly implemented or through airborne, aerosol or dust particles. The rate of infection in dermatological surgery is low and can easily be treated with oral antibiotics. Infection rates are directly proportional to the length of the procedure and certain body sites. Dixon et al. assessed the infection rate in 2424 patients who underwent a wide range of dermatological procedures. They observed an infection rate of greater than 5% in procedures performed below the knee, groin, ear and lip[23]. Hence, the decision to prescribe a prophylactic antibiotic should be based on patient comorbidities and biopsy site.

There is also an increased risk of postoperative infections if poor surgical technique is employed. Examples include too much pressure on sutures, causing ischemia at the site, using too much suturing material, and not shaving body hair at the surgical site. All these lead to higher rates of wound infection.

The role of topical antibiotics has been studied to detect their effectiveness in wound healing and prevention of wound infection. It was demonstrated by Smack et al that the rate of infection between two groups of topical antibiotic ointment and topical petrolatum was equal among 922 patients. The topical petrolatum acted as a wound moisturizer and prevented exposure of the wound to debris and dust particles. The added advantage of using simple petrolatum was that it did not contribute to rising antibiotic resistance [24] . We also employed topical Polymyxin ointment postoperatively at the time of first dressing to give immediate protection to the surgical wound.

According to Akiyama, there was no case of SSI in 75 punch biopsies were one group was given prophylactice antibiotics and other was not [25] . As there was no case of SSI in this study, it is concluded that the role of prophylactic antibiotics in skin biopsy procedures where proper aseptic measures are applied is not warranted. In our study, four patients developed SSI but these were incision and excision biopsies, and no punch biopsy.

Total 04 out of 151 patients developed SSI in our study, 03 of them had comorbid conditions (diabetes mellitus in two patients and smoking in one). Out of 04 infected patients, 03 were biopsied from the trunk and one from the leg. Only 02 patients were elderly diabetics. The other 02 patients were young adults with active lifestyles and they did not take time off from work to rest, which might have contributed to their wounds becoming infected. All cases were treated with a 05- day- course of oral Co-amoxiclav and topical Fucidic acid. The infections resolved without any complications. Due to the very small number of infected cases, the association of wound infection with either comorbid conditions or the site of biopsy could not be established in our study. A study revealed an increase in SSI in the absence of antibiotic prophylaxis but a difference in the size of study group may be the explanation for it [26].

We underscored the importance of strict aseptic measures to preclude the need for oral antibiotic prophylaxis after skin

biopsy. Many international studies have been done to judge the role of oral antibiotics in dermatological procedures. All have reported low infection rates if strict aseptic measures are taken instead of prophylactic antibiotics [10,16,25,26] .

Our study also vindicates the previous international studies. Another factor that we included as a comorbid was the hot and humid environment of Karachi. In theory and practice, we observe increased cutaneous bacterial infections in tropical areas. However, if the procedure is a simple biopsy involving a clean wound, and strict aseptic techniques are employed, the need for prophylactic antibiotics is obviated even in tropical areas.

CONCLUSION

Ensuring strict aseptic measures in skin biopsy procedures can be very helpful in reducing wound infections thus obviating the need for oral or topical antibiotics. Avoiding unnecessary antibiotics in minor surgical procedures such as dermatological surgery will eventually lead to decreased antibiotic resistance.

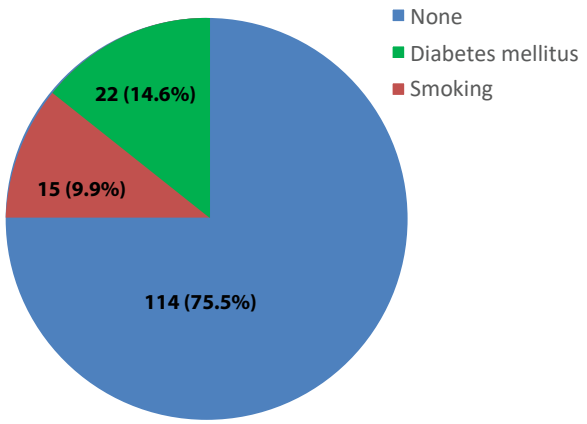

Figure 1: Frequency and percentages of comorbid conditions in the patients

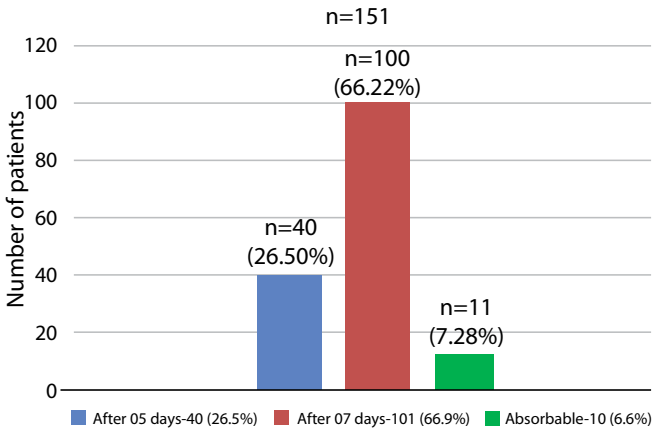

Figure 2: Distribution of patients according to the number of days after which the stitches were removed

Table 1: Frequencies and percentages of sites of skin biopsy

Sr no.	Site of biopsy	Frequency (n=151)	Percentage (%)
1	Head and neck	41	27.2
2	Arms	21	13.9
3	Trunk	45	29.8
4	Groin	5	3.3
5	Legs	29	19.2
6	Nail bed/ matrix	08	5.3
7	Oral mucosa	02	1.3

Table 2: Frequency of wound infection in comorbid conditions

Comorbid conditions	Wound infection		Total
	Yes	No	
None	01	113	114
Diabetes mellitus	02	13	15
Smoking	01	21	22
Total	04	147	151

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AUTHORS' CONTRIBUTION

- ***Jauhar Mumtaz Khan:*** *Drafting the article, acquisition of data, critical revision*
- ***Muhammad Usman Rathore:*** *Analysis and interpretation of data*
- ***Moizza Tahir:*** *Conception and design, Acquisition of data, critical revision*
- ***Waqar Malik:*** *Analysis and interpretation of data*
- ***Ali Riaz:*** *Acquisition of data, Drafting the article*

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ORIGINAL ARTICLE

EFFICACY OF THE COMBINATION OF DACLATASVIR AND SOFOSBUVIR FOR THE MANAGEMENT OF HCV GENOTYPE 3 PATIENTS

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ABSTRACT

Objective: To determine the frequency of sustained virologic response (SVR) of Daclatasvir (DCV) plus Sofosbuvir (SOV) for the management of HCV genotype 3 infections in non-cirrhotic patients.

Study Design: Prospective, observational study.

Place and Duration of Study: Gastroenterology department, Shifa International Hospital Islamabad, 06 months (May to November 2019).

Methodology: Total 75 diagnosed and treatment- naive patients of chronic HCV genotype 3, in whom liver cirrhosis was ruled out by abdominal ultrasound, were included in the study, by non-probability convenience sampling. A combination of DCV (60mg) and SOV(400mg) orally once daily for 12 weeks was given to all and were followed up in the OPD for 12 weeks after treatment. After 12 weeks of completion of treatment, HCV PCR was checked to evaluate the SVR after 12 weeks (SVR-12).

Results: Out of 75 patients, male patients were 56% while female patients were 44%. The mean age was 48.65 ± 13.72 years. Diabetes mellitus was present in 62.7% of the patients. SVR-12 was achieved in 85.3% which showed insignificant association with gender (p-value 0.916), diabetes mellitus (p-value 0.455) and age (p-value 0.076).

Conclusion: Achieving an SVR-12 rate of 85.3% depicts that the combination of DCV and SOV is extremely efficient in treating the HCV genotype 3, Its efficacy is consistent across patients, regardless of age, gender, or diabetes mellitus.

Key words: *Daclatasvir, Genotype, Hepatitis C, chronic, Sofosbuvir, Sustained virologic response.*

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INTRODUCTION

Chronic infection with the Hepatitis C virus (HCV) is a global health concern. The World Health Organization(WHO) recognizes it as a huge public health issue. The estimated worldwide prevalence is 2.8 %, affecting almost 71 million people globally. This Virus can cause acute & chronic hepatitis, liver cirrhosis, hepatocellular carcinoma(HCC), as well as end-stage liver disease(ESLD). The prevalence of chronic HCV in Pakistan is about 6.5% and in some areas, it is around 14%. It is a silent infection, mostly diagnosed when the patient has already developed complications. Almost 20% of chronic cases of HCV present after developing cirrhosis[1,2,3,4,5]. There are about 58 million chronic HCV carriers in the world, according to some recent studies. The disease is causing 290,000 deaths a year[3].

Of the 11 HCV genotypes, found worldwide, HCV genotype 3 is the 2nd most prevalent. Its global prevalence is 30% and even higher than 60% in parts of Southeast Asia[6]. The prevalence of HCV genotype-3 in Pakistan is higher, with a frequency between 75% to 90% of cases[2,7]. This genotype is more aggressive in increasing the risk of liver cirrhosis & HCC[2]. Patients with elevated alanine aminotransferase (ALT) levels, those above

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the age of 18, those with positive HCV RNA, and those with compensated and decompensated liver disease are among those who should receive treatment. Sustained Virologic Response (SVR) is a negative HCV RNA, 24 weeks after the completion of antiviral treatment[2,7]. Late relapse after achieving SVR is extremely low (less than 1%). With an SVR, patients come up with reduced inflammation, fibrosis and liver complications. With SVR reached, HCC and death rate will be very low[2].

Although the direct-acting antiviral agents (DAAs) have contributed to improving SVR, management of those infected with genotype 3, & having compensated or decompensated liver cirrhosis remains difficult. Regardless of treatment history, genotype 3-HCV-related cirrhosis continues to provide a therapeutic challenge. This genotype's inadequate virological response has been linked with higher hepatic steatosis & fibrosis [7,8].

CAPSULE SUMMARY

The combination of Daclatasvir and Sofosbuvir is very effective in treating HCV genotype 3, as evidenced by the high SVR-12 rate in this study. Its effectiveness was constant across patients, irrespective of age, and gender. Effect modifiers had no significant influence.

Recent advancements in HCV infection treatment plans, either alone or in conjunction with Ribavirin and pegylated interferon-alpha, have significantly increased the pharmacological capacity to attain SVR. However, due to the severe adverse effects associated with these drugs, non-compliance is common and patients even discontinue treatment. Among the novel antiviral treatments, a highly effective drug Sofosbuvir(SOV), a pangenotypic NS5B nonstructural protein inhibitor, has recently been approved for treating HCV genotype 3. It works particularly well against HCV genotype 3 when combined with Ribavirin or Pegylated Interferon (Peg-IFN) plus Ribavirin. Another potent option, Daclatasvir (DCV), a pangenotypic NS5A inhibitor, has also demonstrated encouraging outcomes when combined with SOV and Ribavirin[7]. Daclatasvir was approved in 2015 by the Food and Drug Authority to be used in combination with SOV for treating HCV genotypes 1 and 3. Due to the scarcity of alternatives and concerns over their cost, it is still utilised in many government settings. In addition, the government provides it as part of a hepatitis control program[9,11]. Sofosbuvir is prescribed with DCV for the treatment of HCV with/without ribavirin, and treatment has been dramatically changed with the advent of new antivirals[2,10]. In the 2016 ALLY-3 Phase III trial, which compared SOV-DAC combination therapy concluded that SVR is higher in non-cirrhotic patients' treatment-naive about 96% and 86% for treatment-experienced patients[11]. There is a dearth of information on this combination in this region of the world, although few trials have evaluated the safety & efficacy of DAA-based therapy of adult patients having chronic HCV infection, notably regimens based on DCV and SOV with or without Ribavirin[12]. The National Hepatitis Control Program includes DCV, which is administered in conjunction with SOV for 12 weeks to combat genotype 3. DCV was added at the government level, which improved compliance and produced positive treatment results[13].

Given the low effectiveness of antiviral treatment in this subgroup of HCV patients, particularly in genotype 3, analysis of the viral response in de-compensated cirrhosis warrants particular consideration. A small number of advanced liver disease cases have been included in a few trials that have assessed the use of DCV/SOV in genotype 3-HCV-infected patients in clinical practice[14]. The DCV/SOV-based regimen also showed promising results in different coinfections like HIV and special populations like kidney transplant recipients among the immunosuppressive status of patients[15]. From 2020 onwards, the SOV/DCV regimen has become the preferred DAA treatment for HCV in low- & low-middle-income countries, accounting for around 2/3rd of the global prevalence [16].

Pakistan is included in the low-income countries list. Moreover, SOV/DCV regimen is provided at many public hospitals through the National Hepatitis Control Program. Assessing the efficacy of this DAA combination is the foremost rationale of this study in a resource-limited setting like our country. This study assessed the efficacy of combining SOV and DCV for treating HCV genotype 3 infection in our population.

METHODOLOGY

This prospective, observational study was done at the Deptt. of Gastroenterology, Shifa International Hospital, Islamabad, from 24-05-2019 to 24-11-2019. Institutional Review Board provided the ethical approval for this research (Reference number: 421-364-2017, Date: 12-1-2017).

All patients in the age range 18-70 years reporting to the outpatients department (OPD), diagnosed with chronic HCV genotype 3, were screened for cirrhosis by ultrasound abdomen and baseline HCV RNA. Total 75 patients who were non-cirrhotic on ultrasound and had baseline HCV RNA >15 IU/ml were included by nonprobability convenience sampling. All patients were treatment-naive. Pregnant, lactating, patients having cirrhosis, un-typeable genotype and prior hypersensitivity to drugs were excluded.

All data were recorded through structured proforma. After informed consent, demographic information of patients (name, age, gender) was recorded. Basic labs were checked namely Complete Blood Count (CBC), Liver Function Tests(LFTs), Serum Creatinine level & International Normalized Ratio (INR). SVR was operationally defined to be achieved if HCV PCR is <15 IU/ml, 12 weeks after treatment completion. The selected patients were started with DCV 60mg and SOV 400mg orally once daily and were followed up in OPD for 12 weeks. Then the patients were advised to follow-up after 12 weeks of the end of treatment and HCV PCR were checked. The primary endpoint was an SVR after 12 weeks (SVR-12) of the end of treatment, assessed with a sensitive molecular method.

Reports were assessed and HCV RNA<15 IU/mL was labelled as achieved SVR-12. All this information was recorded through structured proforma. All lab investigations were done in the hospital laboratory and were verified by pathologists.

Data analysis was done with SPSS 20. Means & Standard Deviation were calculated for the quantitative variables, and frequencies & percentages for the qualitative ones. Data was stratified for age, gender and diabetes mellitus to deal with the effect modifiers. After stratification, a chi-square test was applied setting a p-value of <0.05 as significant.

RESULTS

The study was done on 75 patients, in order to determine the frequency of SVR-12 of DCV plus SOV combination for the management of HCV genotype 3 infection in non-cirrhotic patients.

The minimum & maximum ages of patients were 25 and 70 years respectively. The mean of the age was 48.65 ± 13.72 years. Male patients were in the majority (56%). Diabetes mellitus was identified in more than half of the patients (62.7%). The SVR-12 was achieved by most of the patients. Table 1 and Figure 1 show the detailed results. A chi-square test determined the association of SVR-12 with gender, age and diabetes mellitus.

Table 1: Characteristics of the study participants.

S.no	Characteristic	Subcategory	Frequency (n=75)	Percentage (%)
1.	Gender	Male	42	56
		Female	33	44
2.	Diabetes Mellitus	Present	47	62.7
		Absent	28	37.3
3.	SVR-12 achieved	Yes	64	85.3
		No	11	14.7

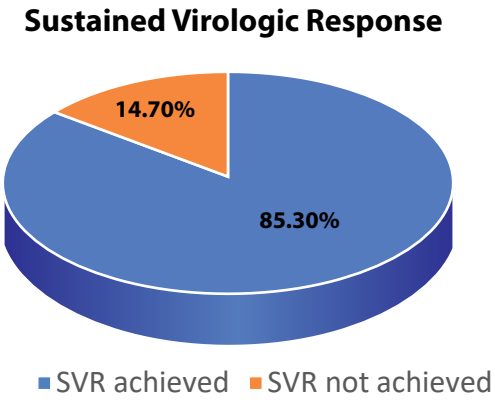

Figure 1: Percentage of sustained virologic response achieved 12 weeks after completion of treatment

Table 2: Association of SRV-12 with different characteristics

Characteristics	Subcategory	SVR achieved n (%)		p – value
		Yes	No	
Gender	Male	36 (48)	6 (8)	0.916
	Female	28 (37.3)	5 (7)	
Age	≥47 years	30 (40)	2 (2.6)	0.076
	<47 years	34 (45)	9 (12)	
Diabetes Mellitus	Present	39 (52)	8 (10.6)	0.45
	Absent	25 (33.3)	3 (4)	

Age was categorized into two groups of > 47 & < 47 years of age. Despite differences in percentages, the analysis showed that gender, age and diabetes mellitus do not have a significant association with achieving SVR. The findings imply that treatment regimens play a more critical role in determining SVR outcomes irrespective of age, gender or presence of diabetes mellitus (Table 2).

DISCUSSION

The frequency of SVR-12 of the DCV plus SOV for the management of HCV genotype 3 infection in non-cirrhotic patients was determined. In our study, SVR-12 was achieved by maximum (85.3%) patients. Our results are comparable to another prospective, observational study, by Jinnah Postgraduate Medical Centre, (JPMC) Karachi [9], which had 300 patients with detectable HCV RNA PCR with the most prevalent genotype 3 (83%). The mean age in their study (40.49 years) was slightly lower than the mean age in ours but the dispersion in the age (SD ± 13.86) was comparable to our results. In contrast to our study, the majority of the patients included were females (58%). Combination therapy with SOV and DCV was administered for either 12 or 24 weeks, with Ribavirin added for treatment-experienced and cirrhotic patients. SVR-12 or SVR-24, was achieved in 88.33% of patients which is slightly higher than the response achieved in our study. Both studies highlight the effectiveness of combination therapy with SOV and DCV across different patient populations and settings. However, differences in demographic profiles such as gender distribution, treatment durations, and patient characteristics, such as cirrhosis, treatment history and presence of Diabetes Mellitus, may account for variations in outcomes. Regardless of these differences, both studies demonstrate high efficacy rates for achieving SVR-12, which supports the utility of this therapeutic regimen in managing HCV.

Another observational study conducted at Lady Reading Hospital, Peshawar, from Jan to Dec 2020, presents insights into the effectiveness of SOV and DCV in achieving SVR in patients with HCV [17]. That study had 172 patients, with a mean age of 40 (SD ± 12.23) years, a little lower than in our study. Age distribution showed that 53% were young adults (18–40 years)

and 47% were middle-aged and elderly (>40 years of age). This age distribution was comparable to our study which showed more patients (57%) in age <47 years. Gender distribution was in contrast to our study showing a majority of the female participants (55.8%). Most of the participants in the study were diagnosed with genotype 3(69.8%) and 91.3% had normal liver on ultrasound. This study achieved slightly higher SVR12 rates than our study (93.6% vs. 85.3%). Gender and age showed no significant association with SVR 12(p-value>0.05) which is comparable to our results. Both studies confirm the high efficacy of the SOV + DCV regimen in achieving SVR12 across various patient groups.

Our results are comparable to another study conducted on 835 patients in a resource-limited country. Mean age of 50.5 ± 13.73 was higher than our study with the same dispersion. In contrast to our study, the most represented age group (42.2%) was 50 – 69 years. A male predominance of 60.78% was comparatively more than our study. The study showed a very high treatment efficacy after 12 weeks of treatment. Result of HCV PCR <15 IU/mL was achieved among 99.4%, which is much higher than our response rate [3]. Our results are comparable to another multicenter study conducted across multiple government and private tertiary care hospitals in Pakistan which evaluated the efficacy of SOV and DCV in achieving SVR in HCV genotype 3 infection [13]. This study was done on 972 patients. The mean age 46.5 ± 13.3 years was slightly lower than our participants with the predominance of female participants. Total 94.4% of patients achieved SVR-12, a comparatively higher response than our study. The slightly lower SVR-12 rate in our study may be due to the differences in sample size, patient characteristics, and comorbidities such as diabetes. In contrast to our study, it showed a significant association of age with SVR-12. Age above 60 years was identified as a significant predictor of non-SVR.

Another study done at the Hepatitis Clinic, Medical Unit–II, Jinnah Hospital Lahore, supports the results of our study that DCV in combination with SOV is an efficient strategy for HCV genotype 3. That study had 135 patients. The mean age of the participants was 49.8 ±2.3 years with a predominance of male participants which is comparable to our results. The SVR-12 was achieved by 91.1% of patients which shows higher response than our study [18].

CONCLUSION

SVR-12 was achieved in 85.3% of HCV genotype 3 infection patients who used the DCV plus SOV combination. Effect modifiers had no significant influence. The combination demonstrated high efficacy & good tolerability in HCV genotype 3 infection in the study population.

Non-probability convenience sampling technique and an inadequate sample size were the main limitations of our study. Future research should concentrate on examining the risk variables linked to treatment failures and a low SVR.

ETHICAL APPROVAL: *Reference number: 421-364-2017, Date: 12-1-2017*
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- ***Sana Tahir Virk:*** *Drafting the article, analysis and interpretation of data*
- ***Sadaf Yousaf:*** *Acquisition of data, Drafting the article*
- ***Kazim Abbas Virk:*** *Conception and design, critical revision*
- ***Zaid Umer:*** *Analysis and interpretation of data*
- ***Abeer Zafar:*** *Acquisition of data, Drafting the article*
- ***Mahwish Ahmad:*** *Conception and design, Critical revision*

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ORIGINAL ARTICLE

COMPLIANCE TO ANTIHYPERTENSIVE TREATMENT AMONG HYPERTENSIVE PATIENTS AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To assess the compliance of hypertensive patients to the treatment prescribed by the physician.

Study Design: Cross-Sectional Study.

Place and Duration of Study: Sheikh Zayed Medical College, Rahim Yar Khan, 01 month (June to July 2023).

Methodology: All patients who presented to the medical outpatients department from June to July 2023 and fulfilled the inclusion criteria were inducted in the study. Predesigned questionnaires were used for data collection. The study subjects were hypertensive patients who attended the outpatient department of the Medical unit of the hospital. The subjects included were at least 20 years old and using antihypertensive drugs for at least 6 months. The non-probability, convenience sampling technique was used for sample collection. The questionnaire included information regarding the sociodemographic status of the participants and questions that assessed compliance to antihypertensive therapy. Data were collected, and analyzed by using SPSS version 23.

Results: Total 190 hypertensive patients were included in the study. Out of 190 study subjects, 88 (46.31%) were found to be compliant to their antihypertensive drug treatment, while 102 (53.69%) were non-compliant. The high cost of the medicines (p=0.04) and forgetfulness (p=0.05) significantly predicted noncompliance to antihypertensive treatment.

Conclusion: The level of compliance to antihypertensive medication was poor in more than half of the hypertensive patients. The significant predictors of non-compliance were forgetfulness and the high cost of medicine.

Key words: *Antihypertensive agents, Compliance, Hypertension.*

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INTRODUCTION

Hypertension refers to an elevated blood pressure. Adhering to the advice given by the healthcare professional regarding the schedule, amount, and frequency of drug use is known as medication compliance. It is measured in relation to a time span[1].

Globally about 1.28 billion people, 30-79 years of age, suffer from hypertension and around two-thirds are from low- and middle-income countries. Forty-six per cent of the hypertensive patients are ignorant of their illness. Approximately 42% of adult patients are diagnosed as hypertensive and are receiving treatment. One in five persons (21%) have controlled hypertension. Hypertension is among the main causes of early mortality across the globe. Increased westernization and urbanization have been linked to the rising incidence of hypertension, with urban regions showing a greater frequency than rural ones. Furthermore, it is anticipated that the prevalence of hypertension will keep rising worldwide. There will be 1.56 billion persons worldwide with hypertension in 2025, which is about a 60% increase from the current estimate[2].

A study showed good compliance in Indian patients[3]. A meta-analysis showed that non-compliance to antihypertensive treatment is high in low to middle-income Asian countries[4]. A cross-sectional study carried out in Faisalabad, Pakistan, revealed similar results, showing poor compliance rates of the antihypertensive treatment among participants[5]. Another study from Pakistan showed that non-compliance could potentially explain poor blood pressure control in the area[6].

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On comparing the earlier research data from Pakistan, frequency was found to be greater among men and in metropolitan regions. The incidence will probably rise over time quickly. Our findings highlight the value of high-caliber, long-term research to better understand hypertension and develop preventive and management strategies[7].

Pakistan has a high rate of urbanization, its citizens consume a high caloric diet, have high salt and saturated fat intake and less fruits and vegetables in their diets. Numerous studies have proposed that these modifications are one of the reasons of hypertension being more common in urban than rural populations. Pakistan must enhance its efforts to prevent hypertension, which calls for the development of a prudent preventative strategy and the strengthening of existing anti-hypertension laws. There is no nationwide research on the disease, the most recent national inquiry was carried out more than 20 years ago. Despite the fact, we took into account several small- to intermediate-scale studies on the prevalence of hypertension from all around Pakistan[7,8].

CAPSULE SUMMARY

Lack of compliance with the prescribed treatment worsens the condition.

In this study compliance with antihypertensive treatment was evaluated at a tertiary care hospital. Predictors of drug compliance were also determinded.

Compliance was found to be poor in more than half of the patients. The important predictors of noncompliance were forgetfulness and the high cost of medicines.

These results collectively suggest that hypertension is and will remain a significant concern for healthcare professionals. Certain lifestyle changes must be made in addition to antihypertensive medications to regulate blood pressure. Some adjustments include dietary changes, smoking cessation, cutting back on drinking, controlling weight gain, increasing physical activity, and managing stress. In addition to lifestyle changes, individuals may need to take one or more antihypertensive medications to effectively regulate their blood pressure. The patients need to take the medication for the rest of their lives[9,10].

The most common consequences of hypertension, such as stroke, coronary heart disease, retinopathy, nephropathy and peripheral vascular disease, can be prevented or delayed with effective management of blood pressure[11].According to a 2022 study, the risk probability of stroke among hypertensive patients was 78.9%, (males 91.0%, females 70.7%), and with the persistence of hypertension, it would increase[12].Although trained healthcare professionals are responsible for teaching patients, each patient is ultimately responsible for adhering to their treatment plan. Merely one-third of hypertensive patients were adhering to their antihypertensive medication, according to a previous study[13,14].

The present study was conducted to assess the compliance of hypertensive patients to the treatment prescribed by the physician.

METHODOLOGY

This cross-sectional, observational research was carried out at a tertiary care hospital, Sheikh Zayed Medical College, Rahim Yar Khan. Ethical approval was sought from the Institutional Review Board (Reference number: 05/RDSU/SZMC, Date: 08-03-2023).

All patients fulfilling the inclusion criteria, and presenting to the medical outpatients department (OPD), from June to July 2023, were included in the study after their informed consent. Predesigned questionnaires were used to obtain data from the patients. The study subjects consisted of hypertensive patients who attended the OPD of the hospital's medical unit. The subjects included were 20 years and above of age, using antihypertensive drugs for at least the last 6 months. The exclusion criteria included patients with hypertension, not receiving medication. A non-probability convenience sampling technique was used for sample collection. The questionnaire included information regarding the sociodemographic status of the participants, and questions to assess compliance with antihypertensive therapy.

The data were collected and analyzed, using SPSS version 23. Noncompliance with antihypertensive medication was labelled when the patient either omitted a single dose or stopped taking antihypertensive medicines altogether. All variables were either numerical or categorized. The chi-square test was applied for the categorical variables, as a test of significance, to determine the association between them. Variables included were sociodemographic e.g. sex, age, marital status, medication, and information regarding health care providers, and were analyzed, with compliance taken as a dependent variable. Some other variables like high cost of medicines, forgetfulness to take medications, availability of free medications in government hospitals, side effects of medication, trust in the efficacy of drugs, incurability of the disease and poor health education were also measured as the predictors of the treatment compliance. Statistical significance was taken at $p<0.05$.

RESULTS

A total of 190 hypertensive patients were included in the study,102 (53.68%) were males and 88 (46.34%)were females. The mean age of the study subjects was 56±12 years. Out of all patients, 88 (46.31%) were married, and 102 (53.69%) were unmarried or widowed. Among the study subjects, 75 (39.5%) were illiterate and the rest had education standards as given in Table 1. Employment status was as given in Table1. Total 88 patients (46.31%) were observed as compliant to the

Table 1: Sociodemographic characteristics of the population

Variable	Frequency (n=190)	Percentage (%)
Sex		
Male	102	53.68
Females	88	46.32
Marital status		
Married	88	46.31
Widowed	82	43.15
Single	20	10.52
Education		
Illiterate	75	39.47
Primary	60	31.57
Matriculation	36	18.94
Fsc and above	19	10.00
Occupation		
Employed	105	55.26
Unemployed	41	21.57
Retired	44	23.15

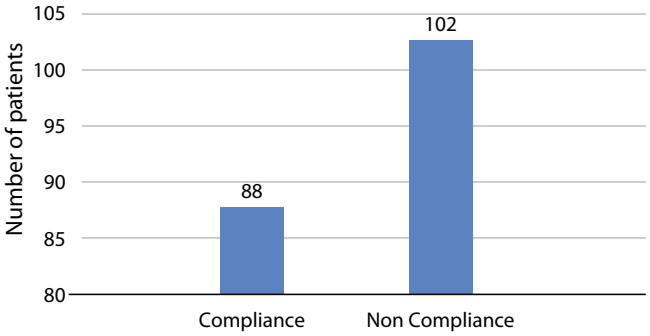

Figure 1: Compliance to Antihypertensive treatment among patients with Hypertension

antihypertensive drug treatment, while 102 study subjects (53.69%) were noncompliant (Figure 1).

The analysis of the predictors of antihypertensive drug treatment noncompliance showed that the high cost of the medicines (p=0.04) and forgetfulness (p=0.05) significantly predicted noncompliance to antihypertensive treatment (Table2).

DISCUSSION

Compliance to antihypertensive drugs treatment is of paramount importance as far as control of hypertension and prevention of disease is concerned[9]. The developing countries are struggling for good healthcare systems and when combined

Table 2: Predictors of drug compliance to antihypertensive medicines

Variables	Odds ratio	95% Confidence interval	p-value
Trust in drug efficacy	3.691	0.152-7.641	0.28
High cost of medicines	1.53	0.617-4.562	0.04
Government hospital drug provision	2.729	0.175-5.138	0.31
Side effects of drugs	0.712	0.019-3.149	0.19
Forgot to take drugs	0.152	0.175-1.629	0.05
Incurability of disease	0.068	0.017–0.274	0.35
Poor health education	1.715	0.451-2.472	0.21

with patient characteristics or attitudes towards health, adherence or compliance rates are very poor[15]. The results of this study showed that 88 (46.31%) study subjects were compliant with the prescribed antihypertensive drug treatment, while 102 (53.69%) subjects were noncompliant. The poor compliance among hypertensive patients in our study is comparable with other regional studies[16]. In one study, out of 306 outpatients with hypertension, 42.2% of patients were compliant with the prescribed medication. Medication adherence was substantially impacted by comorbid diseases($p<0.05$) and multiple medications (p-values <0.05)[17]. Some socioeconomic, demographic, and environmental variables such as age, health and literacy were associated with adherence[18,19]. Multiple variables, like socioeconomic, demographic and clinical factors have been explored in the quest for a more dependable no-adherence prediction. Even in the trials from which the predictive model was derived, composite score produced from several predictive parameters, while statistically significant, does not always result in precise prediction for individual patients[20].

In the current study, a few variables, including trust in drug efficacy, high cost of medicines, incurability of the disease, government hospital drug provision, side effects of drugs, forgetfulness to take drugs, and poor health education, were analyzed as predictors of compliance to the treatment. It was noted that the analysis of the predictors of antihypertensive drug noncompliance showed the high cost of the medicines, (p=0.04) and forgetfulness (p=0.05) significantly predicting noncompliance to antihypertensive treatment. There was a substantial decrease in compliance among the individuals who stated that their medicines were not easily accessible due to high costs. These results were in line with a previous study[21]. Even if the patients had the will but were unable to obtain the prescribed medication were less likely to comply. Participants in the previous studies who had experienced the side effects of the prescribed drugs had less compliance than the patients who had no side effects ever (p=0.19) This was similar to the findings of a study that showed that patients in whom side effects were reported had more chances of stopping the drugs,

resulting in a poor compliance[22]. Some hypertensive patients in that study missed to take the prescribed antihypertensive drugs. However, there was no statistically significant difference between the variables. Previous literature evidenced that adherence to antihypertensive drugs was noted to be sub-optimal, and was determined by the presence of comorbidity, lack of health education, counselling, over-the-counter drug practice and multiple drugs prescribed as a combination for the management of hypertension[23,24].

CONCLUSION

This study showed poor antihypertensive treatment compliance. Less than half of the patients reported compliance with the prescribed drugs. The significant predictors of noncompliance were forgetfulness and the high cost of medicines.

ETHICAL APPROVAL: *Reference number: 05/RDSU/SZMC, Date: 08-03-2023*

CONSENT FOR PUBLICATION: *Written, informed consent was obtained from the study participants.*

AVAILABILITY OF DATA: *Data is available from the corresponding author on a justified request.*

FINANCIAL DISCLOSURE/ FUNDING: *None*

ARTIFICIAL INTELLIGENCE TOOLS DISCLOSURE: *None*

CONFLICT OF INTEREST: *None*

ACKNOWLEDGEMENT: *None*

AUTHORS' CONTRIBUTION

- ***Ghulam Mustafa:*** *Conception and design, critical revision*
- ***Muhammad Zafar Majeed:*** *Drafting the article, acquisition of data, analysis and interpretation of data,*
- ***Manzur Ahmed Manzur:*** *Drafting the article, acquisition of data, analysis and interpretation of data*

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ORIGINAL ARTICLE

COMPARISON OF FREQUENCIES OF ADVERSE FETAL OUTCOMES IN THE THIRD TRIMESTER OF PREGNANCY IN FEMALES WITH AND WITHOUT OLIGOHYDRAMNIOS

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ABSTRACT

Objective: To compare the frequencies of adverse fetal outcomes in females with and without oligohydramnios in the third trimester.

Study Design: Prospective Cohort Study.

Place and Duration of Study: Department of Obstetrics & Gynaecology, Fauji Foundation Hospital, Rawalpindi, six months (Dec 2021 to June 2022).

Methodology: Sample size calculation was done by open epi calculator, with a 95% confidence interval, 80% power of the study and 41.57% anticipated frequency of meconium-stained liquor in patients with amniotic fluid index (AFI) < 5 cm and 13.48% frequency in females with a normal volume of AFI. The calculated sample size was 80 patients. Two groups of 40 patients each were made. One group (Group A) included females diagnosed with oligohydramnios while the other (Group B) included those without oligohydramnios.

Results: The mean ages of the pregnant females were 28.2±5.0 years and 28.3±4.7 years in Group A and Group B respectively. The mean gestational age of Group A was 35.3±1weeks and 36.7±0.6 of Group B. In Group A, 17(42.5%) females were primigravida and 23(57.5%) were multigravida while in Group B, 22 (55%) were primigravida and 18 (45%) were multigravida. It was observed that adverse fetal outcomes such as abnormal Cardiac topography (CTG), presence of meconium, fetal distress and low birth weight were significantly more in Group A than Group B.

Conclusion: Oligohydramnios is significantly associated with adverse fetal outcomes. Once diagnosed, it needs careful evaluation and fetal surveillance in the antenatal and intrapartum periods to reduce perinatal morbidity and mortality.

Key words: *Fetal distress, Infant, low birth weight, Meconium, Oligohydramnios, Pregnancy outcome, Pregnancy trimester, third.*

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INTRODUCTION

Amniotic fluid, the fluid around the fetus in the amniotic sac, is formed from maternal plasma which crosses placental membranes into the sac in early gestation. After embryogenesis, the main source of amniotic fluid is fetal urination. The fetal kidneys begin to produce urine at the end of 1st trimester and the urine production rate continues to increase till term, reaching approximately 1000-1200ml/day[1,2,3.] During the 3rd trimester, major amniotic fluid volume (AFV) comes from swallowing and urination by the fetus. Other sources include fetal gastrointestinal & respiratory tracts, and the umbilical cord, contributing to a 40% increase in AFV. A near-term fetus swallows about 200-450ml/day & urinates about 600-800ml/24hrs[2,3]. It is observed that fetal hemostatic variations affect the volume of fetal urine, swallowing and lung secretions, so AFV reflects the fetal status. Any condition of decreased renal blood flow leads to reduced urine production and oligohydramnios.

Amniotic fluid has the important functions of providing an aquatic cushion and protecting the fetus from internal trauma, decreasing the impact of uterine contractions as well as regulating temperature[1]. The best non-invasive method

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for accurately estimating AFV is ultrasonographically measuring amniotic fluid index (AFI) or single deepest vertical pool (DVP)[4].

Oligohydramnios is reduced liquor volume for a given gestational age. It is defined as AFI <5cm qualitatively or a single DVP of <1 cm quantitatively. The reported incidence of oligohydramnios varies from 0.5%to 5% [5].

CAPSULE SUMMARY

A significant association was found between oligohydramnios and poor fetal outcomes. To lower perinatal morbidity and mortality, close assessment and fetal monitoring after the diagnosis of oligohydramnios are required.

The causes of oligohydramnios can be fetal, maternal or idiopathic. Common obstetrical problems associated with oligohydramnios are hypertensive disorder, dehydration, antiphospholipid syndrome(APS), premature rupture of membranes (PROM), multiple pregnancies, and postdate pregnancy. Fetal causes include renal agenesis and obstetric uropathy in late pregnancy. Oligohydramnios in the third trimester is usually associated with uteroplacental insufficiency due to conditions like preeclampsia and other maternal vascular diseases. It is associated with intrauterine growth retardation (IUGR).

Oligohydramnios in late pregnancy can result in adverse perinatal & maternal outcomes like increased prevalence of induction of labour, emergency lower section cesarean section (LSCS) due to fetal distress, birth weight < 2.5kg, low APGAR score, neonatal hospitalization & neonatal death. The management of late-onset oligohydramnios depends upon the underlying causes. Treatment options in the 3rd trimester include serial transabdominal amino infusions, transcervical infusions, desmopressin, occlusion of the cervical canal with fibrin gel and vesico-amniotic shunting in obstetric uropathy. Maternal oral or parenteral hydration is associated with improvement in AFV, as shown by recent studies.

Oligohydramnios in late pregnancy requires strict antenatal and intrapartum fetal surveillance to reduce fetal morbidity and mortality[6,7].

Local studies are sparse. This study was planned to compare the frequencies of adverse fetal outcomes in females with and without oligohydramnios in 3rd trimester so as it can provide a baseline for making treatment decisions in our own setting.

METHODOLOGY

This prospective cohort study was done over six months, from Dec 2021to June 2022, in the Department of Obstetrics & Gynaecology, Fauji Foundation Hospital, Rawalpindi, Pakistan. Ethical approval was sought from the Institutional Review Board (Reference number: 873/RC/FFH/RWP, Date: 09-12-2021). Sample size was calculated using open epi calculator with a 95% confidence interval, 80% power of study and 41.57% anticipated frequency of meconium- stained liquor in patients with AFI < 5 cm and 13.48% frequency in females with a normal volume of AFI[8]. The total calculated sample was 80 patients. Total 2 groups of 40 each were made. Group A included females diagnosed with oligohydramnios while Group B included those without oligohydramnios.

Inclusion Criteria: Women with singleton pregnancy with AFI <5cm (Group A) and those with AFI >5cm (Group B), and gestational age between 36-40 weeks.

Exclusion Criteria: Women with PROM, hypertensive disorders of pregnancy, systemic diseases such as SLE, APS, diabetes mellitus, vascular diseases, anemia, postdate pregnancy, fetal congenital and chromosomal abnormalities.

All participants were asked about their medical, obstetrical and gynecological history. Patients diagnosed with oligohydramnios were called for antenatal follow-up till delivery and fetal outcomes were evaluated.

Statistical analysis was done with SPSS 20. For quantitative variables, mean ± SD was calculated. Frequencies and percentages were calculated for variables like fetal distress and low birth weight. Chi-square / Fishers exact test was used for the comparison of frequencies of fetal outcomes between the two groups. Significance was taken at p-value of ≤ 0.05. The relative risk was calculated. Effect-modifiers like age, parity and gestational age at birth were controlled by stratification, applying chi-square.

RESULTS

A total of 80 pregnant women were included in this study. Group A included those with oligohydramnios (AFI<5cm) and grouped as exposed while women with AFI >5cm were grouped as unexposed in Group B. The mean age of Group A was 28.2±5 years and 28.3±4.7 years of Group B.

The mean gestational age at diagnosis was 35.3±1.1 weeks in Group A and 36.7±0.6 weeks in Group B. Regarding parity, 17 (42.5%) were primigravida and 23(57.5%) women were multigravida in the exposed group (Group A) while in the unexposed group (Group B) 22 women (55%) were primigravida and 18 (45%) were multigravida. The age group of 18-25 years showed a significant difference in more adverse fetal outcomes than the group having older participants ($p<0.05$). These outcomes show that the age of the mother is a factor involved in the adverse fetal outcomes with oligohydramnios (Table1). When we compared parity with adverse fetal outcomes, there was a significant difference ($p<0.05$) between primigravida and adverse fetal outcomes with oligohydramnios as compared to the group of multigravida and oligohydramnios (Table 2).

Frequencies of adverse fetal outcomes and fetal distress, including abnormal cardiotocography (CTG), and meconium staining were higher in Group A in comparison with Group B (Figure 1). The mean birth weight of the fetus in Group A was

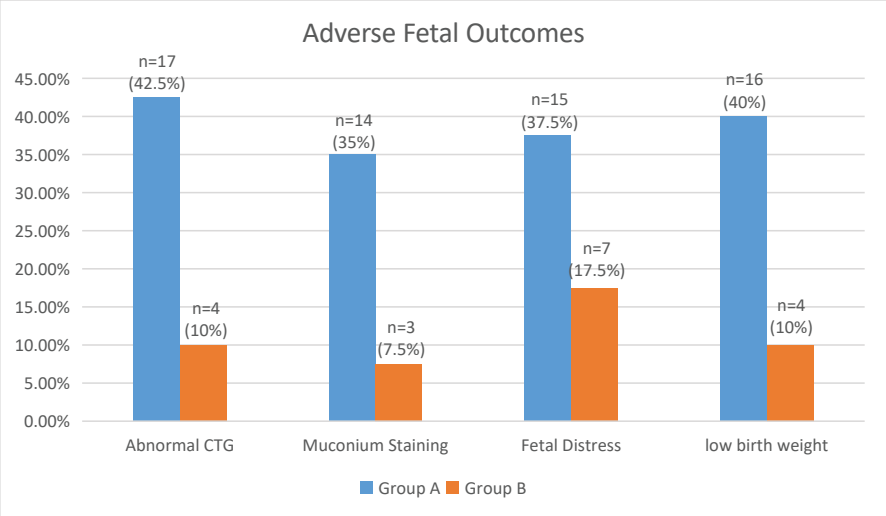

Figure 1: Comparison of adverse fetal outcome in groups.

Table 1: Comparison of Age with Adverse Fetal Outcome.

Age (year)	Group	Adverse Fetal Outcomes n(%)		Total	Relative Risk	p–value
		Yes	No			
18-25	Group A	7 (64)	4(36)	11	6.363	0.05
	Group B	1(10)	9(90)	10		
Total		8	13	21		
26-35	Group A	11(38)	18(62)	29	3.793	0.02
	Group B	3(10)	27(90)	30		
Total		14	45	59		

Table 2: Comparison of parity with Adverse Fetal Outcome.

Parity	Group	Adverse Fetal Outcomes n(%)		Total	Relative Risk	p-value
		Yes	No			
Primigravida	Group A	10(59)	7(41)	17	6.470	0.00
	Group B	2(9)	20(91)	22		
Total		12	27	39		
Multigravida	Group A	8(35)	15(65)	23	3.130	0.11
	Group B	2(11)	16(89)	18		
Total		10	31	41		

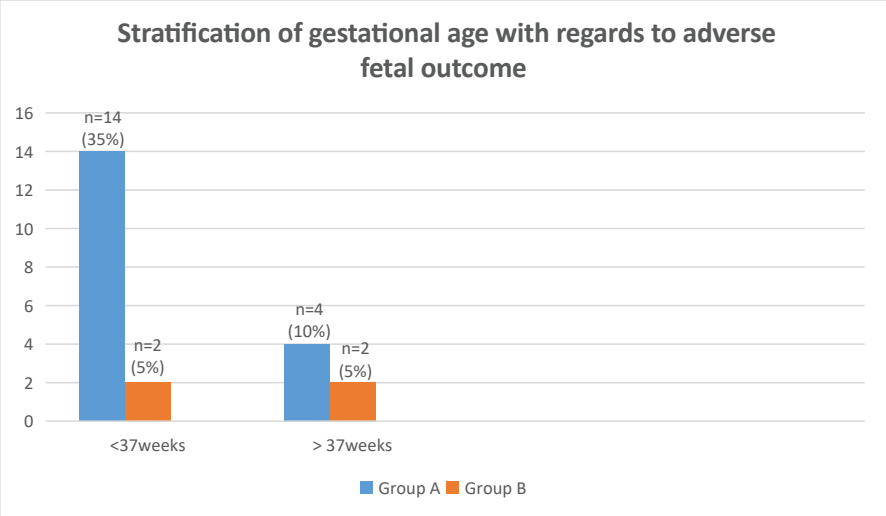

Figure 2: Stratification of gestational age with regards to adverse fetal outcome

2.4±0.05 kg and it was 2.9±0.5 kg in Group B (p-value <0.05).

More adverse effects were noted in fetuses of mothers in Group A with a gestational age of <37 weeks as compared to gestational age of >37 weeks. However, no difference was seen in the fetuses of mothers in Group B (Figure 2).

DISCUSSION

Our study has shown that oligohydramnios at term is associated with adverse perinatal outcomes. In this study 72.5% of women were between 25-35 years of age. Total 42.5% were primigravida while 57.5% were multigravida. A study by Chaudhari KR showed that 65.3% of women were age 20-25 years, 35.8% were primigravida and 64.1% were multigravida [9]. Similarly, a study by Sebastian G showed that 80% of females were 20-30years and 46.3% were primigravida[6]. A study by Bhat S showed that 86% of women were between 20-30 years and 54% were primigravida [1]. Nath J in their study showed that 15 were aged 25-30 years which is in contrast to findings in our study while 36% were primigravida and 64% were multigravida which is compatible to our study [10]. The age group of 18 to 25 years showed significant difference of more adverse fetal outcomes than the group having older participants (p<0.05). These outcomes show that the age of the mother is a factor involved in the adverse fetal outcomes with oligohydramnios. When we compared parity with adverse fetal outcomes, the difference was statistically significant (p<0.05) between primigravida & adverse fetal outcomes with oligohydramnios as compared to the group of multigravida & oligohydramnios.

In the current study, 40% of babies in Group A had low birth weight (< 2.5 kg), abnormal CTG was found in 42.5%, 35% had meconium staining of liquor and frequency of fetal distress was found in 37.5%, while Nath J showed it in 59%, 80% and 13.2% respectively which is in contrast to our study [10]. A study showed that 36% of babies were low birth weight (<2.5kg) which is compatible to our study [1],while contrast results have been found in studies by Nath J (65.38%), Chate P (62%), Chaudhari KR (65.3%) and Seraj A (83%) [10,11,9,5]. A study by Jamal A showed 18.7% low birth weight babies in contrast to our study [12]. Our study showed that 42.5% women in Group A had abnormal CTG. Comparable results were found in study by Chate P that is 38%, 42.3%, in a study by Chaudhari KR while it was 43.6% by Jamal A [11,9,12]. Nath J showed frequency of 66% of abnormal CTG, while VidyaSagar V showed 19.5% which were in contrast to results of our study [10,13]. Meconium staining of liquor was found in 30.7% in a study by Chaudhari KR and 36% by Madhavi K and 31% in a study by Nath J [9,14,10]. These results were comparable to our study. Results in contrast to our study were found in studies by Chate P , Seraj A, Jamal A and VidyaSagar V, 46%,54.7%,17.2%, and 9.7% respectively [11,5,12,13].

CONCLUSION

Oligohydramnios increases the risk of adverse perinatal outcomes including abnormal CTG, thick meconium staining and fetal distress in intrapartum period which may be associated with increased requirement of caesarean sections. These features are more common when associated with low gestational age. It is also observed that oligohydramnios causes a greater risk of low birth weight. Since, it is a frequent occurrence, so early detection, evaluation and extensive antepartum and intrapartum surveillance can improve perinatal outcomes. The variables with adverse fetal outcomes need to be explored with a larger sample size which was one of the limitations of our study.

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AUTHORS' CONTRIBUTION

- **Fatima Anwar:** *Acquisition of data, Drafting the article*
- **Ambreen Fatima:** *Analysis and interpretation of data, Critical Revision*
- **Nadia Bokhari:** *Conception and design, Analysis and interpretation of data*
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ORIGINAL ARTICLE

DEMOGRAPHICS AND COMORBIDITIES ASSOCIATED WITH HYPERTENSION AND PRESCRIPTION PRACTICES BY JUNIOR HOUSE OFFICERS FOR DISEASE MANAGEMENT IN RELATION TO CLINICAL GUIDELINES

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ABSTRACT

Objective: To identify the demographics and most common comorbidities associated with hypertension and evaluate the prescription practices of Junior house officers for pharmacotherapy of hypertension, focusing on standard guideline adherence.

Study Design: Descriptive, Cross-Sectional Study.

Place and Duration of Study: Abbottabad, 03 months(Feburary to April 2021).

Methodology: This study was conducted on 120 hypertensive patients from the in-patient department. Demographic data, comorbidities, treatment regimens, and adherence to Joint National Committee (JNC-8) guidelines were extracted from patient charts. Descriptive statistics were used to assess associated comorbidities and adherence to guidelines.

Results: In our study population, hypertension is found slightly more common in males (52.5%) and in those aged 51-60 years (30%). Diabetes was the most prevalent comorbidity (41.7%) followed by Ischemic heart disease (40%). Vasodilators (66.67%), diuretics (42.50%), and beta blockers (40.83%) were the most frequently prescribed antihypertensive drugs, whereas statins (65.83%) and antiplatelets (56.67%) represented the predominant combination therapies. Only 47.5% of prescriptions complied with JNC-8 guidelines.

Conclusion: Hypertension was commonly reported in male and old age patients. Diabetes mellitus and ischemic heart disease were the most common comorbidities. The majority of junior house officer's prescriptions for hypertensive patients were inconsistent with the established guidelines. This highlights the necessity for targeted educational interventions and enhanced support to improve guideline adherence and treatment outcomes.

Keywords: *Comorbidity, Drug prescriptions, Guideline Adherence, Hypertension.*

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INTRODUCTION

Hypertension is a pervasive global health issue, representing a significant risk factor for severe cardiovascular events, chronic kidney disease, and stroke, particularly where blood pressure management is inadequate[1,2]. Management of hypertension is increasingly intricate in patients with old age and concurrent conditions like chronic kidney disease and diabetes. In these cases, such medications should be prescribed that can control high blood pressure as well as address other comorbidities, in accordance with the standard clinical guidelines to optimize outcomes[3]. For junior house officers (JHOs), who frequently encounter these challenging cases in inpatient settings, an extensive knowledge of standard guidelines for the management of hypertension is important for safe and effective prescribing practices [4].

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Despite the available standard treatment guidelines, research reveals a notable gap in both knowledge and adherence to protocols for hypertension pharmacotherapy among junior house officers[5,6]. Deviations from standard protocols can compromise treatment efficacy and increase the risk of adverse drug reactions, especially in patients with other comorbidities. The selection and dose of medications, particularly with coexisting illnesses, require a precise and evidence-based approach. For instance, Angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) are often prescribed for patients with diabetes for renal protection[7,8]. Meanwhile, additional dose adjustments are required in patients with chronic kidney disease to safeguard kidney function and reduce the risk of potential toxicities[9]. Adherence to evidence-based guidelines and judicious treatment selection enables the JHOs to effectively navigate complexities in hypertension management, ultimately enhancing patient outcomes.

CAPSULE SUMMARY

Hypertension was more common in males and the elderly. Diabetes mellitus and ischaemic heart disease were the most prevalent comorbidities. Most prescriptions by the junior house officers did not adhere to recognised norms. This emphasises the importance of targeted educational initiatives and increased assistance to improve guideline adherence and treatment outcomes.

Recent clinical guidelines by American College of Cardiology/ the American Heart Association (ACC/AHA) and European Society of Cardiology (ESC) emphasize the shift towards patient-centered care, highlighting the necessity of considering patient comorbidities, age, and cardiovascular risk, in decision-making for treatment strategies[1,10]. The initial treatment decisions made by junior house officers(JHOs) have a profound impact on patients' long-term health outcomes, underscoring the importance of considering complex patient factors. In patients with comorbid hypertension and chronic heart failure, beta-blockers and selective ARBs are associated with improved survival and reduced hospitalization rates. Conversely, combination therapy involving thiazide diuretics and ACE inhibitors is efficacious in preventing stroke recurrence in hypertensive patients [11].

This study was planned to find out the demographics and comorbidities associated with hypertension, and to investigate the prescribing patterns of JHOs in managing hypertension among inpatients, with a particular emphasis on adherence to clinical guidelines. This will encourage the development of tailored educational interventions, aimed at enhancing clinical outcomes for hypertensive patients. Given JHOs' critical role in initiating treatment, bolstering their expertise in pharmacotherapy and guideline adherence is crucial for improving patient care quality and mitigating hypertension-related complications.

METHODOLOGY

In this Descriptive cross-sectional study, data was collected between February to April 2021 from a hospital in Abbottabad. The IRB approval was taken from the Department of Pharmacy, COMSATS University, Abbottabad (Reference number: FA16-PHM-060/ATD, Date: 18-1-2021). All patients of both genders, ages over 18 years and diagnosed with hypertension within the specified duration (Feb 2021-April 2021) were included in the study by using a convenience sampling technique. Patients having prescriptions suggested by senior doctors were excluded. Data were extracted from patient charts containing key details such as demographics, chief complaints, laboratory reports (blood pressure, respiratory rate, temperature etc), treatment regimen, and adherence to prescribed medications. The study also included patient comorbidities which influence the choice of pharmacotherapy based on current guidelines.

To guide pharmacotherapy evaluation, the study referred to resources like the British National Formulary (BNF), Eighth Joint National Committee (JNC-8) guidelines, AHA journals, Medscape, Drugs.com, and recent literature via Google Scholar.

A standardized format for collecting data was adopted to document prescription data, treatment categories, and pharmacotherapy regimens uniformly. Multiple variables were analyzed including age, gender, type of hypertension and co-morbidities. MS Office Excel version® 2021 and SPSS version 26 were used to calculate descriptive statistics for all variables.

RESULTS

A total of 120 patient records were analyzed for this study, focusing on individuals diagnosed with hypertension. Among the studied population, a slightly higher prevalence of hypertension (52.5%) was found in males compared to females (47.5) as given in Table 1.

Regarding age distribution, the most prevalent age group among hypertensive patients was 51-60 years, comprising 30% of the total cases. This was followed by the 61-70 year age group, which accounted for 23% of the patients (Table 2).

The analysis of patient complaints revealed a variety of symptoms reported by individuals diagnosed with hypertension. Among these, the most prevalent complaint was chest pain (80%). Other commonly reported complaints included shortness of breath (SOB), fever, and headache. The frequencies and percentages of these complaints are summarized in Figure 1.

The assessment of comorbidities among the study participants revealed that diabetes was the most frequently reported condition (41.7%) followed by ischemic heart disease (IHD) (40%) (Table 3).

Table 1: Gender-wise prevalence of hypertension in study participants

Gender	Frequency (n=120)	Percentage (%)
Male	63	52.5
Female	57	47.5

Table 2: Prevalence of hypertension among participants of different age groups.

Age Groups (years)	Frequency (n=120)	Percentage (%)
21-30	3	2
31-40	15	13
41-50	21	18
51-60	36	30
61-70	28	23
71-80	13	11
81-90	4	3

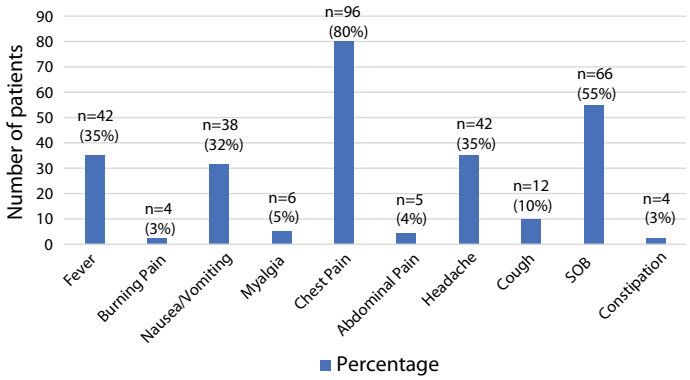

Figure 1: Chief complaints reported by the patients diagnosed with hypertension (n=120).

Table 3: Reported comorbidities in patients presented with hypertension.

Comorbidities	Frequency (n=120)	Percentage (%)
CKD	9	8
Asthma	2	2
MI	30	25
Stroke	6	5
Diabetes	50	42
Dyslipidemia	5	4
IHD	48	40
CHF	13	11

CKD: Chronic kidney disease, MI: Myocardial infarction, IHD: Ischemic heart disease, CHF: Congestive heart failure

Table 4: Antihypertensive and other classes of medication prescribed to the patients.

Medication Class	Frequency (n=120)	Percentage (%)
Antihypertensive		
ACEI	22	18.33
ARBS	21	17.50
CCB	12	10.00
Diuretics	51	42.50
Beta Blocker	49	40.83
Vasodilators	80	66.67
Other Combination		
Anticoagulant	50	41.67
Antiplatelet	68	56.67
Statins	79	65.83
Antidiabetic	40	33.33
PPIS	33	27.50

ACEI: Angiotensin-converting enzyme inhibitor, ARBS: Angiotensin 2 receptor blockers, CCB: Calcium channel blockers, PPIS: Proton pump inhibitors

Table 5: Evaluation of hypertension pharmacotherapy adherence to JNC-8 guidelines.

JNC Guidelines	Frequency (n=120)	Percentage (%)
Followed	57	47.5
Not Followed	63	52.5

Regarding medication profiles, the analysis indicated that various classes of antihypertensive medicines, along with combination therapies, were prescribed to the patients. The major classes of antihypertensives included vasodilators, diuretics, and beta-blockers, with prescription frequencies of 66.67%, 42.50%, and 40.83%, respectively. Statins were the most commonly used adjunctive medication prescribed to 65.83% of patients, followed by antiplatelets and anticoagulants at 56.67% and 41.67%, respectively (Table 4).

The analysis of prescriptions was conducted in accordance with the JNC-8 Guidelines for the management of hypertension. The results showed that about 47.5% of the prescriptions followed these guidelines, whereas 52.5% did not comply (Table 5).

DISCUSSION

This study' findings provide valuable insights into the hypertension-associated comorbidities and pharmacotherapy of hypertension among junior house officers, particularly in the context of adherence to the JNC-8 Guidelines.

Demographically, our study population (52.5% males, 47.5% females) reflects the World Health Organization (WHO's) reported higher hypertension prevalence among males, particularly in middle and old age[12]. The age distribution, peaking at 51-60 years, aligns with epidemiological evidence demonstrating a positive correlation between age and prevalence of hypertension[13]. This age-related association has important clinical implications, as older patients typically present with multiple comorbidities, necessitating nuanced hypertension management strategies.

Our study revealed a high prevalence of diabetes mellitus(41.7%) among hypertensive patients, consistent with the findings of Mannan et al. that diabetes frequently co-occurs with hypertension, thereby significantly increasing the risk of cardiovascular diseases[14]. Presence of additional comorbidities, including CHF and IHD, underscores the importance of implementing comprehensive management strategies that address both hypertension and associated conditions [15].

The prescription pattern in our study revealed a predominance of vasodilators (67%), diuretics (43%), and beta-blockers (41%) as the first-line antihypertensive therapies. This mirrors current clinical practice guidelines, which advocate the use of these medication classes across different hypertension stages, highlighting their therapeutic effectiveness [16]. Our study revealed a notable trend towards a combination therapy, with a substantial proportion of patients receiving concurrent statins, antiplatelets, and anticoagulants[17]. Although combination therapy may offer therapeutic benefits, it also poses risks related to polypharmacy and medication non-adherence [18].

Our findings indicate that approximately 47.5% of prescriptions followed these guidelines, while 52.5% of prescriptions did not. This reveals a notable disparity in hypertension management within the studied population, echoing earlier research that highlighted suboptimal adherence to clinical guidelines among healthcare providers. Consistent with Awan et al.'s observation that 42% of prescriptions deviated from established hypertension treatment guidelines, our study underscores a persistent trend of noncompliance among healthcare professionals [19].

We demonstrated the presence of diabetes mellitus and IHD in patients presenting with hypertension. This study highlights a critical knowledge gap in hypertension management among JHOs, underscoring the need for targeted educational interventions. Enhanced training programs, incorporating seminars and continuous medical education, may improve adherence to clinical guidelines and ultimately enhance patient outcomes. Future studies should elucidate the barriers to guideline adherence and evaluate the effectiveness of educational strategies in diverse healthcare settings.

CONCLUSION

Hypertension was reported more in male and old age patients. Diabetes mellitus and IHD were the most common comorbidities found in hypertensive patients. This study highlights significant gaps in guideline adherence among junior house officers managing hypertension, with only 47.5% of prescriptions aligning with JNC-8 recommendations. The frequent presence of comorbidities, such as diabetes and IHD, underscores the complexity of hypertension management, particularly in older patients. The common use of combination therapies raises concerns about potential polypharmacy issues. To enhance guideline adherence and improve patient outcomes, focused educational interventions and ongoing support for junior house officers are essential. These findings suggest a need for strengthened training efforts in hypertension management within healthcare settings.

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ACKNOWLEDGEMENT: *None*
AUTHORS' CONTRIBUTION

- ***Saqib Khan:*** *Acquisition, Analysis and interpretation of data, Critical revision*
- ***Muhammad Ahsan:*** *Acquisition of data, drafting*
- ***Ayesha Mushtaq:*** *Analysis and interpretation of data , drafting, critical revision*

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CASE STUDY

EASY BRUISABILITY AND FATIGUE IN A YOUNG LADY, DIAGNOSTIC CLUE TO SCURVY : A CASE STUDY

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ABSTRACT

A case of scurvy is reported in a young lady with fatigue, easy bruisability , low mood and cutaneous features suggestive of the clinical diagnosis of Scurvy. This case is presented to remind the young doctors to consider this disease , as it presents insidiously with debilitating repercussions, particularly in the low socioeconomic groups . It can easily be missed, yet is easily treated, therefore high index of suspicion should be kept in the undernourished patients.

Keywords: *Ecchymosis, Malnutrition, Scurvy.*

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INTRODUCTION

Case:

A 28- year- old lady, resident of Multan, presented with multiple ecchymotic patches on the dorsum of feet along with widespread petechial hemorrhages especially involving the lower limbs for 01 month. She reported easy fatiguability and shortness of breath after routine activities for about 4 months. She denied history of fever, photosensitivity, oral ulcers, hematuria, melena and gingival bleed. She was a mother of three and her gynecological history was unremarkable. She managed her household independently and assisted as a helper in two other houses. Her diet primarily based on dairy products, cereals and pulses. She often took Ibuprofen for myalgias and preferred to stay quiet and isolated at home.

On general physical examination she was lean built lady, comfortably sitting. Her BP was 120/60mmHg, pulse 85 beats per minute, respiratory rate 14/minute, temperature 97˚F. Cutaneous examination showed pale, dry skin with enlarged hyperkeratotic hair follicles, palpable purpuric lesions on the extensors of lower limbs and arms. Ecchymosis and linear erythematous streaks, secondary to minor trauma, were seen on the dorsum of feet and legs (Figure 1a & 1b). Gingiva were edematous, with poor oral hygiene and she had dental caries as well. Her systemic examination was unremarkable. Provisional clinical diagnosis of scurvy was made. Her blood complete picture shows Hb of 10.0gm/dl, MCV 70fl. Serum ferritin of 4ng/mL(13-140ng/ml). Antinuclear antibodies (ANA) was negative. She was prescribed Vitamin C 500mg once daily along with dietary advice of taking citrus fruits. She was also given iron supplements. Follow up visit after 2 week showed healed lesions (Figure 2a & 2b) and improvement in fatigue and her general wellbeing.

CAPSULE SUMMARY

A case of scurvy is reported in a young lady who has weariness, easy bruisability, a low mood, and cutaneous characteristics. This case is offered to warn new doctors to examine this disease, as it appears insidiously and has debilitating consequences, particularly in poor socioeconomic groups. It can easily be ignored but is quickly treated; thus, a high index of suspicion should be maintained in the undernourished patients.

DISCUSSION

Sources of vitamin C are vegetables and fruits. Humans cannot synthesize vitamin C, hence dietary intake of citrus fruits, potatoes, tomatoes and green leafy vegetables is essential. Vitamin C is absorbed in the small intestine. This vitamin is required for maturation of triple helix of collagen. Deficiency of vitamin C results in compromised integrity of blood vessels, skin, mucous membranes and bones. It is destroyed at high temperatures during cooking. Deficiency of vitamin C in Pakistani, Indian, Malay and Chinese populations has been seen in comparison to the Western populations and this might increases cardiovascular diseases and cancer among

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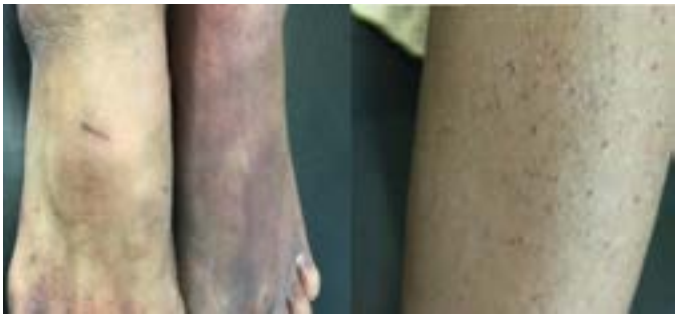

Figure 1a: Ecchymosis on dorsum of feet and hemorrhages on minor trauma.

Figure 1b: Perifollicular hemorrhages and corkscrew hair on leg.

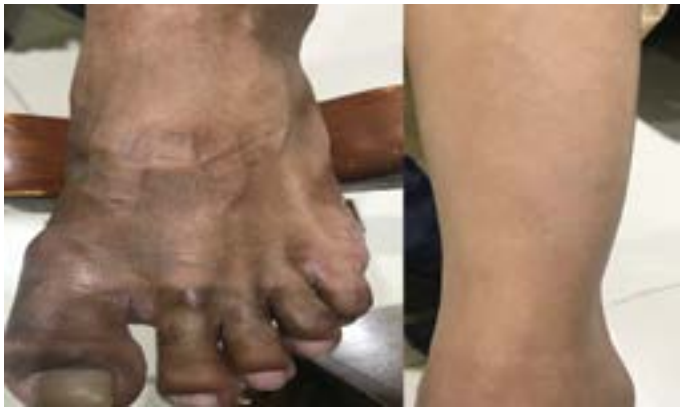

Figure 2a & 2b: Follow up after 2-weeks .

the South Asians[1]. Low vitamin C levels may also be secondary to food choices, genetic predisposition, anemia, pathogens, and nutrient malabsorption[2].

Scurvy manifests when dietary deficiency of Vitamin C persists for several months and reduces thetotal body stores from 1500mg to less than 300mg. Its level in body is regulated by the kidneys ,the excess amount is filtered by the glomeruli and reabsorbed via the tubules to a predetermined threshold. The greatest concentrations are present in the pituitary, adrenals, brain, leucocytes, and the eye[3].

Systemic features of Scurvy are malaise, lethargy, low mood, anemia and edema. Cutaneous features are gingivitis, swollen gums, splinter hemorrhages, corkscrew hair, perifollicular hemorrhages, ecchymosis and follicular hyperkeratosis, painful hemarthrosis, subperiosteal hemorrhage, particularly femur and proximal tibia ,costochondral junction beading – 'scorbutic rosary', intramuscular bleeding and difficulty in walking due to pain. Diagnosis is clinical and recovery occurs with Vitamin C supplementation along with dietary advice. Serum levels of vitamin C reflect a recent intake rather than the body reserves[4]. The recommended dietary allowance is 90 mg/day for men and 75 mg/day for women[5]. Elderly and alcoholics, patients on hemodialysis, those with iron overload, and individuals who had gastric surgery are predisposed to scurvy[6]. Therefore, we must remain vigilant and cautious to recognize scurvy before progression to advanced disease[7].

CONCLUSION

Scurvy is not a disease of the past. We emphasize a thorough history- taking and clinical examination Early treatment can put the patient back to homeostatic health. In addition, the co- existent nutritional deficiencies should be simultaneously treated.

CONSENT FOR PUBLICATION: *Written, informed consent was obtained from the study participants.*
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DIAGNOSTIC CHALLENGE

Check the correct answer on page 72

Case 1

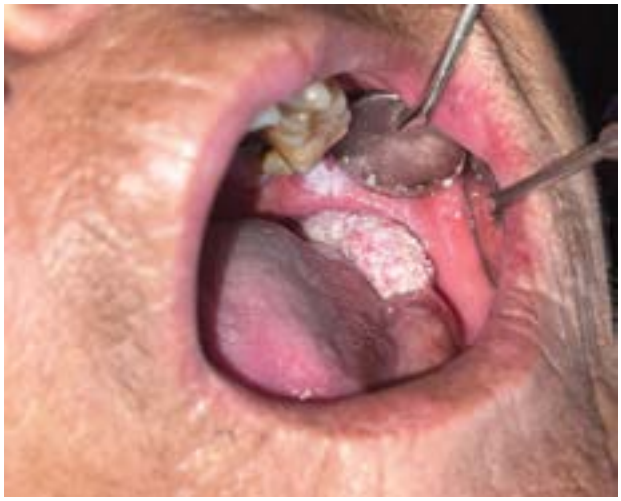

Figure 1

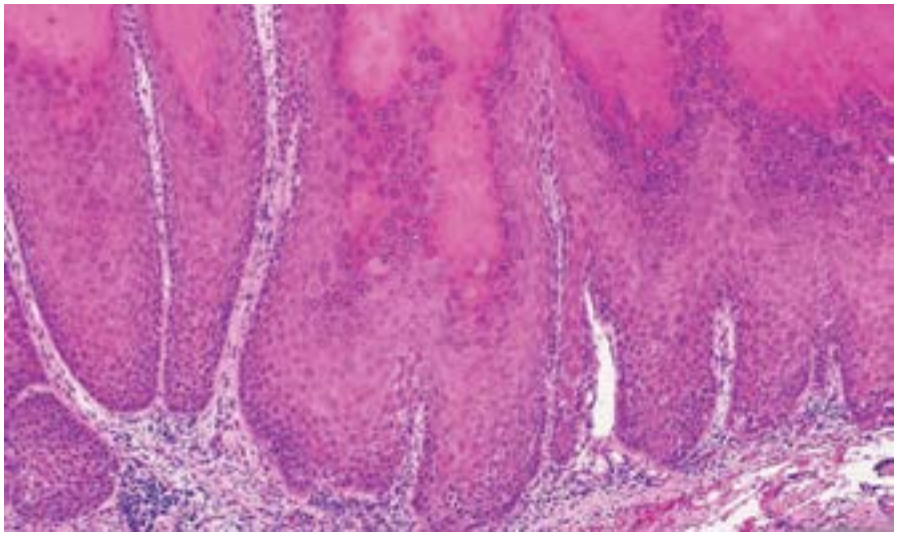

Figure 2

A 72-year-old female presents with gradually enlarging, warty overgrowth on the left buccal mucosa, noted over the past 06 months. She has a history of wearing ill-fitting dentures for 8 years, causing chronic irritation at the site. Examination reveals exophytic, whitish lesions with no ulceration, and no palpable lymphadenopathy (Figure 1). Histopathology is shown in Figure 2.

1. What is the differential diagnosis of the case based on clinical findings?
2. Looking at histopathology what is your definite diagnosis?

DIAGNOSTIC CHALLENGE

Check the correct answer on page 72

Case 2

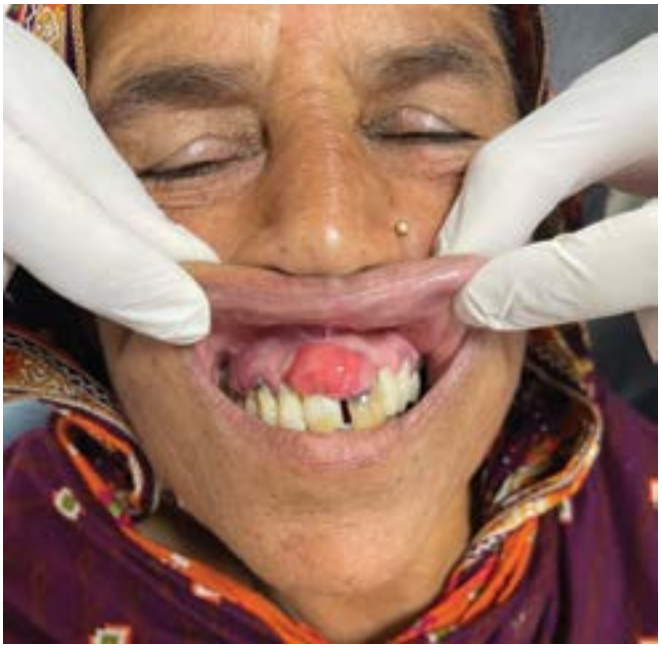

Figure 1

A 52 year old female patient presented with red, swollen growth on my upper gum that bleeds occasionally. The lesion appeared approximately 2-3 months ago and has gradually increased in size. There was mild discomfort but no significant pain. History of the patient revealed poor oral hygiene practices with no associated systemic symptoms. Clinical examination reveals a red, smooth, lobulated growth on the labial gingiva of the maxillary anterior region. The lesion is well-defined, highly vascular with surrounding gingiva showing mild inflammation due to poor oral hygiene (Figure 1). No lymphadenopathy or signs of infiltration were noted.

1. What is the diagnosis of patient?
2. What diagnostic tests are required to confirm the diagnosis?

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DIAGNOSTIC CHALLENGE Answers

Case 1

Diagnosis

Verrucous Carcinoma

Differential diagnosis

1. Verrucous Hyperplasia – Non-invasive, similar appearance.
2. Squamous Cell Carcinoma – More aggressive, ulcerative, infiltrative.
3. Oral Papilloma – HPV-related, smaller, papillary growth.
4. Proliferative Verrucous Leukoplakia (PVL) – Premalignant with potential for VC transformation.
5. Chronic Hyperplastic Candidiasis – White plaques, responsive to antifungals.

Discussion

Verrucous carcinoma (VC) is a low-grade variant of squamous cell carcinoma known for its slow growth, exophytic warty appearance, and locally invasive behavior with minimal metastatic potential. Patients typically present with a painless, slow-growing mass or lesion that may cause discomfort during chewing, speaking, or swallowing, depending on its location. Clinically, Verrucous Carcinoma appears as a whitish or erythematous, well-demarcated lesion with a warty or cauliflower-like surface, often in areas prone to chronic irritation such as the buccal mucosa, tongue, or gingiva. Risk factors include chronic irritation from ill-fitting dentures, tobacco use (smoking or smokeless forms), HPV infection, poor oral hygiene, and long-standing precancerous conditions like leukoplakia or oral submucous fibrosis.

Diagnosis is based on clinical examination and histopathological analysis. The lesion typically shows papillary architecture, hyperkeratosis, minimal cellular atypia, and a "pushing" invasive pattern into connective tissue rather than the infiltrative margins seen in conventional squamous cell carcinoma. Imaging such as CT or MRI may be used to assess local invasion in advanced cases. Treatment primarily involves surgical excision with clear margins, as this ensures complete removal. Radiation therapy is used cautiously due to the risk of anaplastic transformation. Adjunctive care includes addressing modifiable risk factors like replacing ill-fitting dentures and tobacco cessation. With appropriate treatment, Verrucous Carcinoma has an excellent prognosis due to its low metastatic potential, but regular follow-up is crucial to detect any recurrence.

Our Patient

Our Patient had the typical features of verrucous carcinoma with no lymph node involvement.Incisional biopsy of the patient was performed to confirm the diagnosis.Surgical excision was done with clear margins.The patient is kept on follow up to check for any signs of recurrence.

Answers

Case 2

Diagnosis

Pyogenic granuloma

Discussion

Pyogenic granuloma is a benign, reactive vascular lesion commonly occurring in the oral cavity, characterized by a red, smooth, or lobulated growth that is highly vascular, often ulcerated, and bleeds easily. Despite its name, it is neither pyogenic nor granulomatous, arising as a response to local irritation, trauma, hormonal changes, or poor oral hygiene. It is frequently found on the gingiva, particularly in the maxillary anterior region, but can also appear on the lips, tongue, or buccal mucosa. The lesion ranges in size from a few millimeters to several centimeters and may grow rapidly initially before stabilizing. While typically painless, it can cause discomfort or interfere with speech and eating if large or ulcerated. Common triggers include plaque, tartar, trauma from sharp teeth, dental appliances, or hormonal fluctuations, particularly during pregnancy, where it is referred to as a "pregnancy tumor." Histopathologically, it consists of granulation tissue with numerous blood vessels, inflammatory cells, and fibroblastic stroma, often with surface ulceration. Diagnosis is based on clinical examination, imaging to rule out bony involvement, and biopsy to confirm atypical presentations. Management involves removing irritants through scaling and improving oral hygiene, with surgical excision often required to prevent recurrence, along with histopathological confirmation. Adjunctive therapies such as laser excision or cryotherapy may also be used, and regular follow-ups are essential. The prognosis is generally good with appropriate treatment, though recurrence may occur if underlying irritants or hormonal triggers are not addressed.

A biopsy of the lesion is essential to confirm the diagnosis and rule out other conditions like peripheral giant cell granuloma, squamous cell carcinoma, or fibroma. Intraoral periapical (IOPA) or panoramic X-rays can help assess underlying bone involvement or rule out bony lesions.

Our Patient

There was no bony involvement of the lesion. Surgical excision of the lesion was performed along with scaling and polishing to remove local irritants and avoid recurrence.

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