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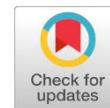
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Research Article

⁶Open Access



Early Postoperative Complete Heart Block after Congenital Heart Disease Surgery: A Two Centre Study in Benghazi

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Abstract

Congenital heart disease (CHD) is a common congenital anomaly that requires surgery. A complete heart block (CHB), which can be temporary or permanent, might complicate surgery for CHD. Objectives: to measure the frequency of early postoperative CHB and assess the contributing risk factors among children with CHD who underwent surgery. A retrospective study of 158 patients with CHD who underwent surgery at the National Heart Centre (NHC) and Benghazi Medical Centre (BMC) between December 2021 and March 2023 and underwent evaluation for an incident of CHB in the postoperative intensive care unit (ICU), was carried out. Data collection from patients' medical records included type of CHD, mortality rate, bypass and aortic clamping time, and hypothermia during operation. Transient CHB occurred in 4.4% of patients, and permanent CHB occurred in 0.63%. The age of patients ranged from less than 6 months to 30 years. The surgical procedures associated with CHB included sub-aortic membrane (SAM) (20%), atrioventricular septal defect (AVSD) (16.6%), and ventricular septal defect (VSD) (7.1%). The mortality in patients with postoperative CHB was (5%). Other comorbidities, including the duration of cardiopulmonary bypass (CPB) and aortic clamping time, have an important effect on the risk of developing CHB. Reducing the bypass time during surgery can reduce CHB.

Keywords: Complete Heart Block (CHB), Congenital Heart Disease (CHD), Children, Risk factor, Pacemaker, Mortality.

INTRODUCTION

Injuries to the atrioventricular (AV) following cardiac surgery for CHD occur in 0.7%–3% of patients. The primary risk factors for cardiac arrhythmias are being young at the time of surgery, undergoing a specific surgical procedure, and enduring long durations of bypass or aortic cross-clamp. These abnormal cardiac rhythms lead to lengthier hospital stays and the need for medical or surgical treatment (Altaweel et al., 2018). In a previous study, Murray and his colleagues (2017) (Murray et al., 2017) noticed that preoperative factors, including a missense polymorphism in GJA5, are independently associated with an increased risk for CHB. (Romer et al., 2019) discovered that specific surgical procedures, including atrioventricular canal defect (AVC), left ventricular outflow tract obstruction resections, and ventricular septal defect (VSD) repair, have been linked to an increased risk of permanent CHB. The block can be induced by trauma or suture placement in



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the conduction system, or hemorrhage or edema from the suture surrounding the conduction system, particularly in younger patients. Previous research by (Azab et al., 2013) showed that 14 out of 400 patients (3.5%) developed permanent postoperative CHB. Improved surgical techniques and enhanced knowledge of the anatomy of conduction tissue in different congenital heart defects reduced this risk to 1–4% (Ahmed et al., 2023; Liberman et al., 2016).

Many studies suggest that minimizing CPB duration during open heart surgery can help reduce the incidence of CHB among children with congenital heart disease (Alotaibi et al., 2022). The patient's age at the time of operation considerably affects the possibility of acquiring a complete heart block. Younger patients have a higher chance of developing complete heart block post-surgery, (Ibrahim et al., 2023). Higher CPB times and hypothermia during operation have been linked to an increased risk of CHB. Hypothermia has been linked to a variety of physiological effects, including alterations in heart function and rhythm and increasing the risk of arrhythmias such as heart block. Additionally, hypothermia can influence the autonomic nervous system, causing alterations in heart rate and rhythm (Shah et al., 2021). The use of inotropes in children with congenital heart defects after open heart surgery entails various concerns, including an increased risk of complete heart block and arrhythmias, an increased risk of low cardiac output syndrome, and mortality. (Gocoł et al., 2021). Temporarily pacing patients to allow the resolution of CHB prevents the excessive insertion of PPMs in patients who will experience a return of conduction (transient CHB). While this waiting period may serve to preempt the need for prolonged hospital and cardiac intensive care unit (CICU) stays, which may result in increased patient morbidity and expenses, it may also result in the superfluous implantation of PPMs in patients with transient CHB (Ju et al., 2023). Consequently, determining the optimal timing for postoperative PPM insertion could decrease patient risk and resource consumption (Liberman et al., 2016; Moskowitz et al., 2019).

This paper aims to study the frequency of early postoperative CHB in patients with congenital cardiac diseases and assess the contributing risk factors among children with congenital heart disease (CHD) who underwent surgical correction.

MATERIALS AND METHODS

This descriptive-retrospective study was conducted at two hospitals, Benghazi National Heart Center (NHC) and Benghazi Medical Center (BMC), on 158 cases operated for CHD from December 2021 to March 2023. The hospital records were reviewed, and demographic and perioperative variables were abstracted, with particular attention to the postoperative condition status of patients in the postoperative intensive care unit. Data collection included age, sex, type of CHD, mortality rate, 12-lead electrocardiogram, and echocardiogram; operative details included surgical details including clamping time and cardiopulmonary bypass time; use of an inotrope; and continuous rhythm monitoring was maintained for the duration of the patient's ICU stay.

Inclusion criteria: Each patient had a normal preoperative 12-lead electrocardiogram (ECG) and another ECG on the first day, 7 days postoperatively, and 10 days postoperatively. All patients at risk of postoperative heart block receive transient pericardial pacing during surgery, and CHB was researched. Eventually, temporary pacing was continued for a maximum of 10 days when the patient developed a heart block. If a return to normal rhythm within 10 days post-operatively

is not restored, the diagnosis of permanent CHB was confirmed according to recommendations from the American College of Cardiology, American Heart Association, and Heart Rhythm Society (ACC/AHA/HRS 2018) (Shah et al., 2021). Patients with a preoperatively complete CHB or a pre-existing PPM were excluded from this study.

Statistical analysis was done using SPSS v28 (IBM Inc., Armonk, NY, USA). Quantitative variables were presented as frequency and percentage (%). Estimating the relationship between a dependent variable and one or more independent-tailed variables with a P value < 0.05 was considered statistically significant.

RESULTS

Regarding the baseline characteristics of the studied patients, 89 (56.33%) patients were males, and 69 (43.67%) patients were females; the median age was 4 (2–7) years. Five (Transit CHB no. 5). Permanent (CHB no. 1) out of eight (75%) patients with CHB were between the ages of one and two years, Table 1.

Table (1). Age at operation.

Age	N (%)	Transit CHB N (%)	Permanent CHB N (%)
1 month - 1 Year (Infant)	38(24%)	1(0.6%)	0(0%)
> 1 year - 2 years (Toddler)	84(53%)	5(3.2%)	1(0.6%)
>3 years - 5 years (Preschooler Age)	18(11.3%)	0(0%)	0(0%)
>5 years - 12 years (School-Age Child)	13(8.2%)	1(0.6%)	0(0%)
>13 years - 19 years (Adolescents Age)	4(2.5%)	0(0%)	0(0%)
>19 years (Adult)	1(0.6%)	0(0%)	0(0%)
Total	158	7(4.4%)	1(0.6%)

Among the studied patients, 106 (67.1%) had cyanotic CHD, and 52 (32.9%) had cyanotic CHD. The surgical procedures associated with the highest incidents of heart block included subaortic membrane (SAM) (20%), atrioventricular septal defect (AVSD) (16.6%), and ventricular septal defect (VSD) (7.1%).

Data are presented as frequency (%). CHD: Congenital heart disease, ACHD: Acyanotic congenital heart disease, CCHD: Cyanotic congenital heart disease, VSD: Ventricular septal defect, ASD: Atrial septal defect, AVC: Atrioventricular canal defect, PDA: Patent ductus arteriosus, AS: Aortic stenosis, COA: Coarctation of the Aorta, AA: Interrupted aortic arch, MR: Mitral regurgitation, SAM: Subaortic membrane, TOF: Tetralogy of Fallot; TGA: Transposition of the great arteries; DORV: Double outlet right ventricle, PS: Pulmonary stenosis, PA: Pulmonary atresia, TAPVD: Total anomalous pulmonary venous drainage, CHB: Complete heart block, PPM: Permanent pacemaker.

The overall mortality rate from CHD surgery was 12 (7.6%). Deaths from CHD surgery associated with CHB occurred in three patients out of 60 who were operated on for VSD and AVC, with transient CHB (5%) and no fatality in patients who underwent SAM resection.

The intraoperative sheet of each patient was revised for the cross-time and bypass, and the procedures were performed on or off bypass, Table 3.

Table (2). Type of operated CHD and rates of CHB and mortality rate in each type of CHD.

Type of operated CHD (n=158)	N (%)	Transit CHB	CHB with PPM	Mortality Rate N/158(%)
A cyanotic CHD	106(67.1%)	7(4.4%)	1(0.9%)	6(3.8%)
cyanotic CHD	52(32.9%)	0(0%)	0(0%)	6(3.8%)
VSD	42(26.58%)	3(7.1%)	0(0%)	1(0.6%)
ASD	26(16.46%)	0(0%)	0(0%)	0(0%)
AVC	18(11.3%)	3(16.6%)	0(0%)	2(1.3%)
PDA	1(0.63%)	0(0%)	0(0%)	0(0%)
AS	4(2.53%)	0(0%)	0(0%)	1(0.6%)
COA, Interrupted AA	7(4.4%)	0(0%)	0(0%)	1(0.6%)
MR	3(1.9%)	0(0%)	0(0%)	0(0%)
SAM	5(3.16%)	1(20%)	0(0%)	0(0%)
TOF	22(13.92%)	0(0%)	0(0%)	3(1.9%)
Sever PS	8(5.06%)	0(0%)	0(0%)	1/(0.6%)
Single ventricle	66(3.8%)	0(0%)	0(0%)	0(0%)
DORV	3(1.9%)	0(0%)	0(0%)	0(0%)
Other Types of CCHD	12(7.6%)	0(0%)	0(0%)	3(1.9%)
TAPVD	1(0.63%)	0(0%)	0(0%)	0(0%)
Total	158	7(4.4%)	1(0.6%)	12(7.6%)

Table (3). Operative data of the studied patients.

Intraoperative Sheet	Total (n=158)
Cross time	Less than 25 min 54 (34.18%) More than 25 min 80 (50.63%) No cross time 24 (15.19%)
Bypass	On bypass 131 (82.91%) Off bypass 27 (17.09%)
Bypass time	<30 min 11 (6.96%) >30-60min 50 (31.65%) >60-90 min 50 (31.65%) >90 min 20 (12.66%) No bypass 27 (17.09%)

Regarding the type of arrhythmia, sinus rhythm occurred in 116 (73.42%) patients, junction arrhythmia occurred in 14 (8.86%) patients, transient CHB occurred in 7 (4.43%) patients, permanent CHB occurred in 1 (0.63%) patient, sinus bradycardia occurred in 2 (1.27%) patients, and SVT occurred in 1 (0.63%) patient, Table 4.

Table (4). Type of postoperative arrhythmia in examined patients.

Arrhythmia	Total (n=158)
Sinus rhythm	116 (73.42%)
Junction arrhythmia	14 (8.86%)
Transient CHB	7 (4.43%)
Permanent CHB	1 (0.63%)
Sinus bradycardia	2 (1.27%)
SVT	1 (0.63%)
Atrial arrhythmia	2 (1.27%)
Ventricle tachycardia	6 (3.8%)
RBBB	6 (3.8%)
Ventricle ectopic	3 (1.9%)

Data are presented as frequency (%), CHB: Complete heart block, SVT: Supraventricular tachycardia, and RBBB: Right bundle branch block.

Table (5).Relation between CHB and other parameters.

				CHB		P value
				ACHD n=106	CCHD n=52	
Inotropes	Dopamine			12 (11.4%)	1 (1.9%)	0.003*
	Dopamine + Adrenaline + Milrinone			2 (1.9%)	5 (9.4%)	
	Adrenaline + Noradrenaline			0 (0%)	1 (1.9%)	
	Milrinone			27 (25.7%)	12 (22.6%)	
	Dopamine + Adrenaline			27 (25.7%)	10 (18.9%)	
	Milrinone + Adrenaline			25 (23.8%)	18 (34.0%)	
	Noradrenalin			0 (0%)	3 (5.7%)	
	Milrinone + Adrenaline + Noradrenaline			1 (1.0%)	2 (3.8%)	
No Inotropes			11 (10.5%)	1 (1.9%)		
Mortality and Type of Postoperative Arrhythmia n=158						
Sinus rhythm 5 (3.1%)	Junction Rhythm 4 (2.5%)	Transient CHB 3 (1.9%)	Permanent CHB 0 (0%)	SVT 0 (0%)	<0.001*	
Hypothermia				42 (40.0%)	19 (35.8%)	0.613
Bypass	On bypass			93 (88.6%)	38 (71.7%)	0.008*
	Off bypass			12 (11.4%)	15 (28.3%)	
Bypass time	<30 min			10 (9.5%)	1 (1.9%)	<0.001*
	>30-60min			44 (41.9%)	6 (11.3%)	
	>60-90 min			27 (25.7%)	23 (43.4%)	
	>90 min			12 (11.4%)	8 (15.1%)	
	No bypass			12 (11.4%)	15 (28.3%)	
Cross time	Less than 25 min			46 (43.8%)	8 (15.1%)	<0.001*
	More than 25 min			50 (47.6%)	30 (56.6%)	
	No cross time			9 (8.6%)	15 (28.3%)	
Infection	Wound infection			2 (1.9%)	2 (3.8%)	0.683
	Mediastinitis			2 (1.9%)	0 (0%)	
	Sepsis			2 (1.9%)	1 (1.9%)	
	No infection			99 (94.3%)	50 (94.3%)	
Mechanical ventilation	< 1 day			21 (20.0%)	6 (11.3%)	<0.001*
	<3 days			5 (4.8%)	14 (26.4%)	
	3-7 days			2 (1.9%)	4 (7.5%)	
	> 7days			0 (0.0%)	2 (3.8%)	
	Exudate from OR			77 (73.3%)	27 (51.9%)	
CNS complica- tion	Convulsion			4 (3.8%)	4 (7.5%)	0.621
	Hemiparesis			1 (1.0%)	1 (1.9%)	
	Delirium			1 (1.0%)	0 (0%)	
	No			99 (94.3%)	48 (90.6%)	
	No			38 (36.2%)	30 (56.6%)	
Peritoneal dialysis				0 (0.0%)	6 (11.3%)	0.001*

ACHD: a cyanotic congenital heart disease, CCHD: cyanotic congenital heart disease, CHB: Complete heart block,
PPM: Permanent pace maker.

Table 5 reveals a statistically significant relationship between CHB and mortality regarding the type of postoperative arrhythmia, inotropes, bypass time, cross time, mechanical ventilation, and

peritoneal dialysis ($P < 0.05$). There was no statistically significant relationship between CHB and the other parameters (hypothermia, infection, and CNS complications).

DISCUSSION

CHB is a notable complication of surgery for CHD. Patients with postoperative CHB need to last ten days following the surgery in the ICU, and if the heart block has not recovered, the replacement of the artificial pacing system is necessary for the duration of the patient's life. CHB might be permanent or temporary; in this context, transient CHB typically returns to sinus rhythm within seven to ten days following surgery. In comparison, 2093 patients (5%) in the study conducted by (Loomba et al., 2024) experienced an atrioventricular block, and 480 patients (1%) required pacemaker insertion. (Romer et al., 2019) reported that patients with transient AVB had 50% recovery within two days and 94% resolution within ten days, and the duration of cardiopulmonary bypass, a high-risk operation, was an independent risk factor for PPM compared to AVB resolution. This finding was also reported in research by (Öztürk et al., 2021). AV block was found in 3.4% of cardiac surgery patients, and all patients fully recovered within the first 10 days. The incidence of early postoperative heart block was noticed to be between 0.7% and 3%, depending on the type of surgical procedure and the cardiac lesion (Khosroshahi & Samadi, 2020; Liberman et al., 2016). We conducted a retrospective review of early and delayed atrioventricular conduction block after surgery for congenital heart disease. Postoperative atrioventricular conduction block occurring in 21 (2.3%) of the 922 patients was noted to be transient, with a return of conduction (1–14 days) after surgery in 13 (1.4%) and PPM (6–20 days) after surgery in 8 patients (0.9%). (Aziz et al., 2013) conducted a monitoring assessment of 44 patients who underwent cardiac surgery and experienced transit CHB in 37 patients and recovered between 5 and 9 days postoperatively. In the current study, the postoperative findings were transit CHD in 7 (4.4%) and AVB with PPM in 1 (0.6%), which are consistent with earlier investigations. Our patients (95%) recovered within 8 to 10 days post-surgery.

The atrioventricular (AV) node is an essential part of the cardiac conduction system; the His bundle (and its divisions) are located within the ventricular septum, thus rendering it susceptible to injury during surgical procedures in the septum. In previous studies by (Azab et al., 2013; Hejazi et al., 2019), they found the incidence of CHB higher in surgical repair of VSD, atrioventricular canal defects (AVCD), double outlet right ventricle (DORV), tetralogy of Fallot (TOF), and subaortic stenosis SAS. Due to the risk of block development over time, postoperative CHD surgery patients require close observation and continual monitoring.

In our study, the surgical procedures associated with the highest incidents of heart block included subaortic membrane resection (SAM) (20%), atrioventricular septal defect repair (AVSD) (16.6%), and ventricular septal defect closure (VSD) (7.1%). This is consistent with earlier findings, as the atrioventricular node is located in a particular location known as the Koch triangle, which is prone to damage during surgical procedures involving that area. In the current study, 1 patient from 42 (2.4%) patients with VSD surgery departed from the hospital with PPM. In contrast to the research of (Sugrue et al., 2018), they reveal that atrioventricular block is prevalent following tetralogy of Fallot (TOF) repair operations because the surgical areas are near the conducting system. Our patients undergoing TOF repair did not suffer from AVB and were more prone to junctional ectopic tachycardia. This could have been explained by the fact that the conduction system was spared during the surgical procedure. Although prior studies appear to support the literature regarding the longer durations of aortic clamp time and cardiopulmonary bypass time in cases with CHB, the observed difference of only a few minutes during a relatively simple procedure involving an isolated

VSD suggests that additional surgical factors and instrument manipulation in the surrounding area of the AV node contribute to the development of CHB (Socie et al., 2017).

The current study found younger ages (53% of patients with CHB) were between the ages of one and two years, consistent with a study concluded by (Ibrahim et al., 2023) where younger ages were a significant risk factor for complete heart block.

The current study showed that there was a significant relationship between CHB and inotropes and bypass time, cross time, mechanical ventilation, and peritoneal dialysis ($P < 0.05$). There was an insignificant relationship between CHB and the other parameters (hypothermia, infection, and CNS complications). ($P > 0.05$), which is similar to studies by (Madani et al., 2023; Socie et al., 2017), who revealed that longer CPB duration and crossing time due to a high-risk procedure were associated with postoperative AVB conditions, in comparison to the study carried out by (Ayyildiz et al., 2016), they found that there was no effect of cardiopulmonary bypass time, cross-clamp time, or preoperative arrhythmia on the development of transit or permanent heart block ($P > 0.05$).

Deaths following CHD surgery associated with CHB (5%). This figure is approximately in agreement with the study done by (Feins et al., 2022), whose reported mortality rate was 3.9% following CHD surgery associated with CHB.

This study has certain limitations; it was a retrospective review of records utilizing reachable medical data. Our review is further restricted by a lack of data about decision-making about the timing of PPM placement, in addition to the relatively small number of patients in this research compared to other researchers due to the lack of continuing programs for open-heart operations for CHD and the dependency on foreign missions.

Finally, this study excluded an assessment of long-term AV nodal conduction; therefore, those who have received PPM placement for postoperative AVB and later returned to normal sinus rhythm, as well as patients who developed late-onset AVB after discharge and required PPM, were not included.

CONCLUSIONS

Postoperative transient CHB represented 4.4% of congenital cardiac surgery complications in the current study, and 0.6% of patients had permanent pacemaker implantation. Within 10 days, 95% of patients with transient CHB had resolved. The overall mortality rate for operated CHD was 7.6%. Death following CHD surgery associated with CHB occurred in VSD and AVC (5%). Reducing morbidity and mortality linked to postoperative CHB requires the creation and implementation of management regimens for patients with CHB, as well as specific types of CHD like AVSD and VSD, aortic clamp time, and cardiac bypass duration, which are predictive variables of CHB.

The study obtained ethical approval from the heads of the pediatric departments at the National Heart Centre (NHC) and Benghazi Medical Centre (BMC) to publish this paper.

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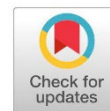
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Research Article

6 Open Access



Antibiotic Prescribing Treatment for Acute Gastroenteritis and Respiratory Illnesses among Children in Al-Bayda, Libya: A Cross-sectional Descriptive Study

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Abstract

Acute gastroenteritis and respiratory illnesses pose substantial morbidity and mortality risks among children under the age of 10. This investigation aimed to assess the prescribing patterns of antibiotics in managing respiratory illnesses and acute gastroenteritis in children. Employing a descriptive, cross-sectional design, data were collected over 6 months from the pediatric unit at Al-Jamee Hospital in Albayda, Libya. Children under 10 years old presenting with symptoms indicative of cough, cold, and diarrhea were included. Patient records were scrutinized for data retrieval, and statistical analyses were conducted utilizing frequencies, percentages, and student t-tests, with significance set at $P < 0.05$. The study encompassed 100 patients with a mean age of 7.6 ± 0.8 years. Predominantly, admissions were prompted by fever (30.5%) and cough or cold symptoms (15.7%). Notably, antibiotic prescriptions exhibited higher appropriateness rates in cases of diarrhea (75.5%; $P < 0.05$). Ceftriaxone (59.5%) and ampicillin (32.4%) emerged as the most frequently prescribed antibiotics. Furthermore, the seniority of the prescriber significantly correlated with prescription appropriateness ($P < 0.05$). The investigation revealed a notable propensity for antibiotic utilization during the management of cough, cold, and diarrhea in pediatric patients in Albayda, Libya.

Keywords: Antibiotics; Children; Common Cold; Diarrhea; Medication Consumption; Prescribing Treatment.

INTRODUCTION

The deliberate utilization of antibiotics presents a global concern. Data from the World Health Organization (WHO) indicates that over 50% of medications are prescribed, dispensed, or sold inappropriately, contributing to incorrect administration in half of patients (Carpenter et al., 2008). Non-optimal medication use manifests in various forms, including overuse, underuse, and misuse of both prescribed and over-the-counter drugs (Karras et al., 2003). Factors contributing to irrational medication practices include suboptimal antibiotic prescription quality (Medalla et al., 2021), inappropriate application of antibiotics in non-bacterial conditions, poor patient adherence, and the emergence of antibiotic resistance. Antibiotics are extensively employed in managing prevalent clinical conditions among pediatric patients (Thielman & Guerrant, 2004; Bresee et al., 2012; Medalla et al., 2021). Research approximates an annual prescription rate of 150 million antibiotics



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in the United States, with 30 million prescribed for pediatric patients (Hay et al., 2016; Denny & Loda, 2010). Observed antibiotic therapy predominates pediatric prescription practices (Shane et al., 2017; Abujnah et al., 2015). While antibiotics play a critical role in treating acute and chronic infectious diseases, their irrational use poses significant risks, such as super-infections and multi-drug resistance (Medalla et al., 2021; Karras et al., 2003). Notably, methicillin-resistant *Escherichia coli* and *Staphylococcus aureus* have developed resistance to multiple antibiotics (Karras et al., 2003). Antibiotic resistance prolongs patient infectiousness, heightening the risk of disseminating resistant microorganisms. Ensuring appropriate antibiotic prescriptions is imperative to foster judicious antibiotic utilization.

Pneumonia and diarrhea constitute the leading causes of mortality in children under 10 years old, according to WHO data (Bresee et al., 2012). These conditions, along with respiratory illnesses, contribute substantially to morbidity and mortality in developing nations, with one in five child deaths attributed to diarrhea or respiratory diseases. Diarrhea ranks as the third most common cause of childhood mortality worldwide, claiming an estimated 300,000 lives annually (Wu et al., 2018). Despite concerted efforts such as universal programs targeting diarrheal diseases and acute respiratory infections, Libya continues to grapple with unacceptably high burdens of diarrhea, cough, and cold morbidity (Abujnah et al., 2015). National and state-level guidelines are available in Libya for managing cough, cold, and diarrhea in children under 10 years old. The Ministry of Health of Libya has issued comprehensive guidelines addressing these conditions (McCullough et al., 2017). These guidelines align with national policies aimed at mitigating antimicrobial resistance, as established by the directorate general of health services. Recommendations include oral rehydration solution and zinc supplements for acute diarrhea, with antimicrobials such as metronidazole, cefotaxime, and ceftriaxone indicated for chronic diarrhea and dysentery (Wu et al., 2018). Similarly, for the common cold and cough, antibiotics are not advised, while azithromycin and amoxicillin are recommended for pneumonia, and ampicillin, meropenem, and gentamicin, for severe pneumonia (Shane et al., 2017). Previous studies focused on examining antibiotic usage in the Pediatric Department and prescribing behaviors for antibiotics in cases of acute diarrhea among the general population (Wu et al., 2018). This research aimed to evaluate the prescription practices and adequacy of antibiotic administration for the management of cough, cold, and diarrhea among children under the age of 10 years.

MATERIALS AND METHODS

A descriptive, cross-sectional inquiry spanning 6 months from July 2023 to January 2024 was executed. This investigation was conducted within the confines of inpatient pediatric units encompassing a general ward and an Intensive Care Unit (ICU) at Al-Jamee Hospital in Albayda, Libya. All children under 10 years of age admitted to the inpatient department exhibiting symptoms indicative of diarrhea, cough, and cold were enrolled as participants. Prospective candidates are identified through a daily check of patient profiles. A team of registered pharmacists systematically collected data using a prearranged form on a daily basis. The content validity of the data collection instrument was ascertained by a panel comprising four healthcare professionals, including two pharmacists and two physicians, who assessed the relevance and significance of the content. Their feedback was assimilated prior to finalizing the data collection tool. Comprehensive data was acquired through a meticulous review of patient profiles, medication records, and associated documentation. In instances where information interpretation posed challenges, on-duty resident physicians were consulted for clarification. Stringent confidentiality measures were upheld throughout the data collection process. Clinical data e.g., symptoms, primary complaints, pertinent medical history, onset time of diarrhea, cough, and cold, diarrhea frequency, presence of fever, vomiting, and respiratory

difficulties were meticulously documented in the data collection as well as from demographic data, age, gender, weight, date of admission, and discharge. Information pertaining to the prescribed antibiotics, including dosage, and route of administration, was also transcribed from the patient medication chart by the designated data collectors. Subsequently, the gathered data underwent a comprehensive assessment for adherence to established criteria based on the Medication Appropriateness Index (MAI) (Scallan et al., 2011). Various parameters including indication, efficacy, dosage regimen, potential drug interactions and drug-disease interaction, feasibility of instructions, availability of cost-effective alternatives, redundancy with other medications, and treatment duration were meticulously evaluated. The data was coded and entered into SPSS version 20 for statistical analysis, with findings presented through frequencies and percentages. The association between dependent variables, such as prescription appropriateness, and independent variables, namely prescriber designation and disease conditions, was examined utilizing the student t-test, with significance set at $P < 0.05$.

RESULTS

During the study period, a total of 100 patient profiles were examined. The mean age of the patients was 7.6 ± 0.8 years. There was a predominance of male children, comprising 63 individuals (58.4%), compared to 37 female counterparts (42.3%). The primary reasons for admission were fever ($n = 55$, 30.5%), followed by cough and cold ($n = 40$, 15.7%), nausea and vomiting ($n = 35$, 22.2%), and diarrhea ($n = 73$, 60.7%), with abdominal pain being the least reported complaint. Notably, abdominal pain and respiratory tract infections were commonly associated with diarrhea and the common cold, respectively. A significant proportion of children (67.22%) had a history of medication use prior to admission. Pseudoephedrine hydrochloride was frequently used for the common cold, while a combination of diphenoxylate with atropine and ondansetron was a common medication for diarrhea and vomiting. Clinical assessment revealed common cold (67.3%) and diarrhea (75.5%) as the predominant clinical presentations. The analysis also indicated a high rate (93.5%) of antibiotic prescriptions in cases associated with common cold and diarrhea. All data are presented in Tables 1, 2, and 3 respectively.

Table:(1). Demographics of the participant population

Variables	Mean $\pm$ SD, or numbers (%)
Age (years)	7.6 $\pm$ 0.8
Gender, number	
Male	63 (58.4%)
Female	37 (42.3%)
Main complaint, n	
Cough and cold	40 (15.7%)
Fever	55 (30.5%)
Nausea and vomiting	35 (22.2%)
Diarrhea	73 (60.7%)
Abdominal pain	12 (3.6%)
Asthma	25 (10.3%)

SD: Standard deviation

Table:(2). Patient medical history

Variables	Number (%)
Medical history	
Yes	76 (85.32%)
No	24 (14.21%)
Medical history	
Yes	37 (67.22%)
No	63 (34.12%)

Table:(3). Clinical evaluation

Clinical evaluation	Number (%)
Common cold	75 (67.3%)
Diarrhea	82 (75.5%)
Asthma	33 (20.5%)
Pharyngitis	25 (10.3%)

The data indicated that ceftriaxone was prevalent among the commonly prescribed medications, accounting for 70 prescriptions (59.5%). Additionally, ampicillin ranked second with 55 prescriptions (32.4%). Gentamicin was notably the most frequently prescribed antibiotic, accounting for 57 prescriptions (25.7%). In contrast, azithromycin was in 28 prescriptions (18.3%). Comparatively, ciprofloxacin, with or without metronidazole combination, represented the least prescribed medication, in only 11 prescriptions (4.5%). This information is succinctly presented in Table 4.

Table:(4). Type of antibiotics prescribed for respiratory and gastrointestinal symptoms

Antibiotics	Number (%)
Ceftriaxone	70 (59.5%)
Ampicillin	55 (32.4%)
Gentamicin	57 (25.7%)
Azithromycin	28 (18.3%)
Ciprofloxacin	11 (4.5%)

DISCUSSION

To date, this study represents a new effort in assessing the prescription leanings and suitability of antibiotic usage among pediatric patients presenting with cough/cold and diarrhea in Albayda, Libya. Its findings promise a substantial contribution to understanding antibiotic utilization patterns in pediatric populations within the region, offering valuable insights for future research endeavors. The majority of children admitted to the hospital were male (58.4%) compared to female children (42.3%) as shown in Table 1. The outcomes reveal a notable prevalence of antibiotic administration among children under 10 years old suffering from cough/cold and diarrhea, aligning with findings from similar investigations conducted in other developing countries (Denny & Loda, 2010; Edwards et al., 2013). The elevated frequency of antibiotic prescriptions raises concerns regarding potential irrational usage practices, which can exacerbate resistance issues, as evidenced in prior research discussions (Emukule et al., 2014). Discrepancies between observed prescription patterns and WHO guidelines underscore potential deficiencies in healthcare provider awareness and institutional policy implementation (Wu et al., 2018). Notably, the frequent prescription of cephalosporins warrants attention due to its implications for healthcare outcomes and resistance concerns, a tendency observed in analogous studies.

Nonetheless, discrepancies in antibiotic appropriateness were noted, with prescriptions for diarrhea exhibiting better adherence to guidelines compared to those for respiratory distress, contrasting findings from prior research (Buzaid et al., 2011). Possible explanations for these disparities include diagnostic uncertainties and limited familiarity with treatment protocols among healthcare providers (Shane et al., 2017). Addressing these challenges necessitates the development of comprehensive policies, including medication review processes, guideline establishment, and regular educational initiatives for prescribers (Periáñez-Párraga et al., 2012; Troeger et al., 2018). These findings echo similar observations from studies conducted in Libya and Northern Tanzania (Mohammed et al., 2016; Nair et al., 2013), emphasizing the pivotal role of healthcare provider qualifications and ongoing medical education in promoting rational antibiotic prescribing practices (Atia et al., 2020). While this study boasts several strengths, including its comprehensive assessment of antibiotic appropriateness across different pediatric conditions, limitations inherent in its design should be acknowledged (Thielman & Guerrant, 2004). Nonetheless, its pioneering nature in evaluating antibiotic appropriateness in cold, cough, and diarrhea among pediatric populations is a notable strength, offering valuable insights for future research and clinical study.

CONCLUSION

In general, a substantial proportion of antibiotics were administered for cough/cold and/or diarrhea in Albayda, Libya. The adherence of prescribed antibiotics to established guidelines exhibited variability according to the specific clinical contexts. Ceftriaxone emerged as the predominant drug of choice among pediatric patients. The implementation of ongoing educational initiatives such as workshops or symposiums focusing on disease management and antibiotic prescription in pediatric populations may serve to promote the rational use of antibiotics.

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ETHICS

Written consent was obtained from the patient's attendants, and authorization to utilize prescriptions for research endeavors was obtained from the Head of the Department of Pediatrics at Al-Jamee Hospital.

Duality of interest: We declare that there are no conflicts of interest regarding the publication of this research study.

Author contributions: This work was carried out in collaboration between all authors. Y. M. designed the study, wrote the protocol, and collected the data. N. I. wrote the manuscript, performed the statistical analyses, and managed the literature reviews. All authors reviewed and approved the final manuscript.

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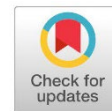
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Research Article

Open Access



CT Stages of Breast Cancer in Newly Diagnosed Libyan Patients

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Abstract

The main objective of this study was to look into Libyan female breast cancer patients' delayed diagnosis and how it affected their disease stage. The study relied on a multidetector CT scan to check for distant metastases because a PET scan was unavailable. According to the study highlighted in this thesis, 43.9% of patients received a diagnosis more than six months after their initial test, with a median diagnosis time for women with breast cancer being 4.9 months. According to the CT scan stages of breast cancer, the clinical stage distribution was 21% stage IV, 35.9% stage III, 34.4% stage II, and only 8.8% stage I. An important factor contributing to the delay in diagnosis was the recipient's inappropriate reassurance that the lump was benign. The delay in diagnosis was associated with a significantly larger tumor size ($p<0.0001$), positive lymph nodes ($p<0.0001$), and a higher incidence of late clinical stage ($p<0.0001$). According to the results of this study, delay in diagnosis is a major concern in Libya and is related to multifaceted interactions between a set of variables which can result in advanced cancer stages and potentially high mortality rates. To encourage early detection, screening centers must be set up and breast cancer awareness campaigns must be elevated.

Keywords: Libyan, Breast Cancer, Tumor Staging, Diagnosis, CT scan.

INTRODUCTION

Breast cancer is the second most common cancer in the world, with 1.67 million new cases diagnosed in 2012. It is the most frequent cause of cancer death in women in less developed regions (324,000 deaths, 14.3% of all cancer deaths), and it is now the second cause of cancer death in more developed areas (198,000 deaths, 15.4%) after lung cancer (Abulhair, O. et al. 2010). In Libya, breast cancer is the most frequent and fatal neoplasm among females. Breast cancer patients often present with an advanced stage, have early disease recurrence, and are associated with high mortality (DeSantis, C. et al. 2013).

A majority of cancers in Africa are predominantly advanced stage at diagnosis because of a lack of screening and early detection services, as well as limited awareness of early signs and symptoms of cancer among the public and health care providers (CO, C. 2008). In the US, death rates from breast cancer in women have dropped since 1990, due in part to early detection by mammography screening and improvements in treatment. Presently, 60% of breast cancers are diag-



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nosed at an early stage, for that, the five-year survival rate is 98% (Andersen, R. S. et al. 2009). If cancer is detected early, within a comprehensive cancer control plan, a significant number of cancer patients can be cured, or have their lives prolonged significantly. If diagnosis is delayed, treatment costs rise substantially, resources are used inefficiently, and the need for palliative care services increases unnecessarily (Arndt, V. et al. 2002).

MATERIALS AND METHODS

Patients: A retrospective review of the medical records of 262 female Libyan patients, ages 25 to 84, who received a new diagnosis of breast cancer at Benghazi Medical Center between 2013 and 2014, was conducted. **Techniques:** To screen for distant metastasis, the study used a multi-detector CT scan (a 64-slice, third-generation Philips CT scan with 42 detector modules; a PET scan is unavailable). Figures 1 and 2 depict the CT staging of a patient with stage IV distant metastases from breast cancer. On a form (questionnaire), retrospective preclinical and clinical data were gathered from patient medical records.

Social and demographic information, medical and obstetric history, questions about symptoms, and questions about consultations were all part of the data collection process. Dates of the sequential occurrences (first symptom recognition, initial consultation, referral, and initial visit to the hospital) were mentioned. Days were estimated for the diagnosis process and any delays. Initial signs and symptoms included a lump, symptoms other than breast pain, symptoms unrelated to the breast, history of oral contraceptive use, and hormone replacement therapy. Information on tumor stage was gathered from each patient's medical records and was based on histopathological (T, N) and clinical (M) data (Arndt, V. et al. 2003).

Based either on FNAC (fine needle aspiration cytology) or histopathological examination (including needle biopsy or excisional biopsy), the diagnosis time was calculated from the date of the first symptoms to the date of the final breast cancer diagnosis. Consultation time was the time spent seeing a general practitioner following the onset of symptoms.

Statistical analysis

We used three months as the cut-off point of delay and divided the diagnosis time into three periods: less than three months, three to six months, and more than six months (Ahmed, S. B. et al. 2002). If the final diagnosis of breast cancer was made more than three months after the onset of symptoms, the diagnosis was deemed to have been delayed (diagnosis delay).

Sociodemographic factors such as age, education level, and work status were thought to be potential predictors of diagnosis delay. Health factors that were believed to have an impact on how long it took to diagnose someone included being menopausal, using oral contraceptives, self-examination of the breast, having a history of fibrocystic disease, and having a family history of breast cancer. SPSS for Windows (version 18, SPSS, Inc., Chicago, USA) was used to analyze the data.

To determine the significance of the data, the Fisher's exact test, the Chi-square test with likelihood ratio (LR) was used. We aimed to identify independent determinants of diagnosis delay of 3 to 6 months and more than 6 months versus less than 3 months, as well as the relationship between possible predictor factors and diagnosis delay. Based on the results of the CT scan, the relationship between the clinical stage and diagnosis delay was investigated for each patient. Values $p < 0.05$ were considered statistically significant in all tests.

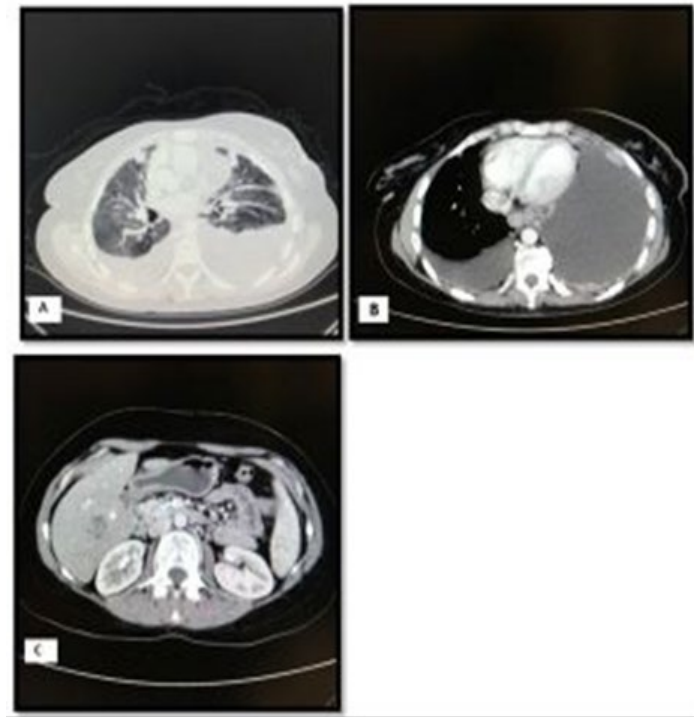


Figure (1). Selected images from the CT examination of a left-sided breast cancer patient with distant metastasis (Stage IV). These axial images through the lower chest and upper abdomen reveal bilateral lung nodules representing lung metastasis (A). Bilateral pleural effusion with nodular pleural thickening is more evident on the left side representing pleural metastasis (B). Heterogeneous enhanced mass in the liver represents liver metastasis (C).

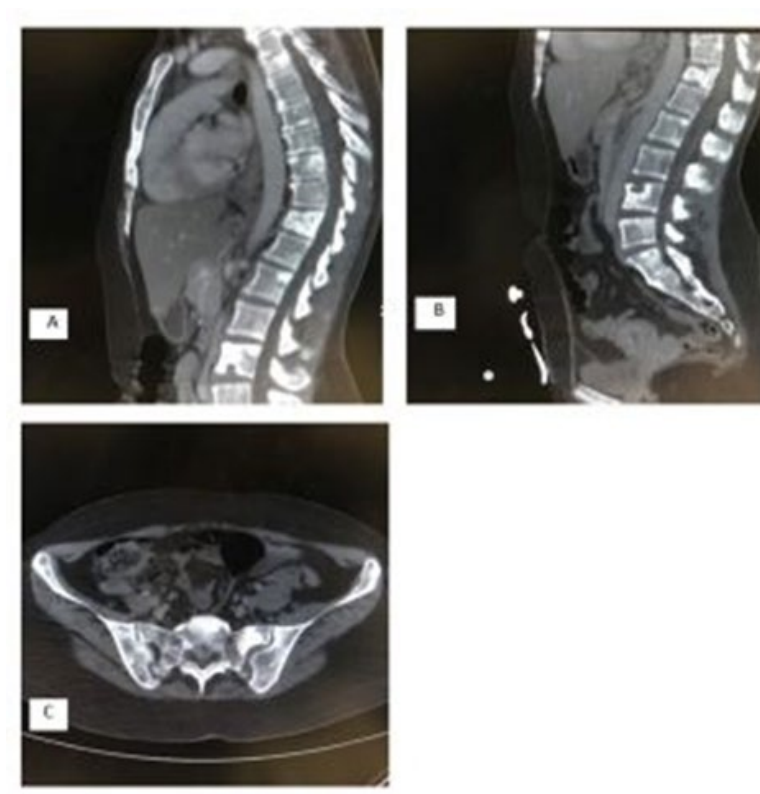


Figure (2). Other selected images from the same patient. Sagittal reformatted images from a CT scan of the spine and axial image of the pelvis reveal diffuse osteosclerotic lesions representing bony metastasis (A, B, and C).

RESULTS

A total of 395 patients with primary breast cancer that had been histopathologically confirmed were admitted to Benghazi Medical Center during the study period. A total of 262 breast cancer patients were included in the study after 133 patients were excluded, 26 patients who were not from Libya, 61 patients with incomplete data, 44 patients who were referred from other cities and had incomplete data with stop follow-up, and two patients who were dead (diagnosed as late stage at age > 50) but had incomplete data. Table 2 displays the characteristics of the study population (n = 262). Women's ages ranged from 25 to 84 years old, with a mean age of 47.8. 166 of the patients, or 63.4%, were literate. Among the 199 patients, 76% were married. Out of 73 patients, 27.8% had used oral contraceptives, and 35.9% of them had gone through menopause. While 7.6% had a history of benign breast disease, only 16% had a family history of breast cancer. In this study, 255 patients (97.3%) who had breast cancer reported discovering a lump or lumps by accident, whereas 7 patients (2.7%) found a lump or lumps while doing a self-examination. Less frequently (19.5%) were reports of other breast symptoms, such as skin changes, nipple discharge, or bleeding. Systemic involvements were the initial symptom in 19 (7.3%) of the patients.

Table (1). Description of the study population (n = 262)

Social demographic characteristics of the patients			
		No. of patients	Percentage %
Age (years)	<50	170	64.9%
	≥50	92	35.1%
Education	Literate	166	63.4%
	Illiterate	96	36.6%
Occupation	Housewife	172	65.6%
	Employed	90	34.4%
Marital status	Married	199	76%
	Single	63	24%
Medical history of the patients			
Menopausal status	Pre-menopausal	168	64.1%
	Post-menopausal	94	35.9%
Breastfeeding	Yes	160	61%
	No	39	14.9%
Oral contraceptive	Yes <5 years	36	13.7%
	Yes > 5 years	37	14.1%
	No	189	72.1%
	Yes	7	2.7%
Breast self examination	No	255	97.3%
Family history	Positive	42	16%
	Negative	220	84%
History of benign breast disease 7.6	Yes	20	7.6%
	No	242	92.4%
Clinical presentations of the patients			
Symptoms	Lump	192	73.3%
	Nipple discharge	17	7.5%
	Skin changes	34	13%
	Systemic	19	7.3%
Symptoms	lump	192	73.3%
	Others	70	26.7%

Diagnosis delay and consultation time

The diagnosis time is displayed in Figure 3. The maximum diagnosis time was 25 months, with a median of 4.9 months. Within three months of the onset of symptoms, 36.6% (n = 96) of the patients received a diagnosis. Diagnoses were made for 19.5% (n = 51) of patients in less than three to six months and 43.9% (n = 115) in more than six months. Four months was the median consultation duration, with a maximum of twenty-four months. In the month following the onset of symptoms, 25.2% (n = 66) of patients saw a doctor, and in the month following symptoms, 39.7% (n = 104) went to the doctor. 92 patients, or 35.1% of the total, saw a doctor more than six months after the onset of symptoms. Most patients (97.3%; n = 255) received their diagnoses within a month of seeing their general practitioners. 2.3% of patients (n = 6) received a diagnosis between one and six months following their initial visit to the physician; 4.4% of patients had to wait longer than six months following their initial medical consultation to receive a diagnosis.

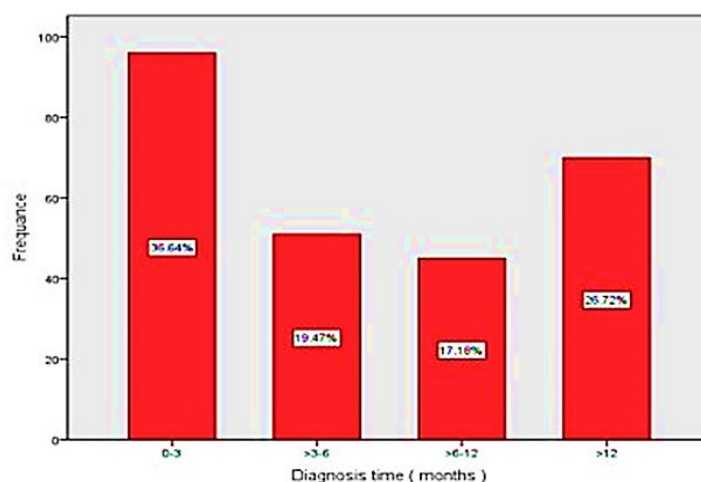


Figure (3). Diagnosis time (from first symptoms) among 262 Libyan breast cancer patients (2013–2014). Diagnosis time (months).

Clinical staging at diagnosis:

8.8% of patients in stage I, 34.4% in stage II, 35.9% in stage III, and 21% in stage IV at the time of diagnosis. Figure 4 displays the clinical stage distribution at diagnosis, and Table 2 shows the TNM staging.

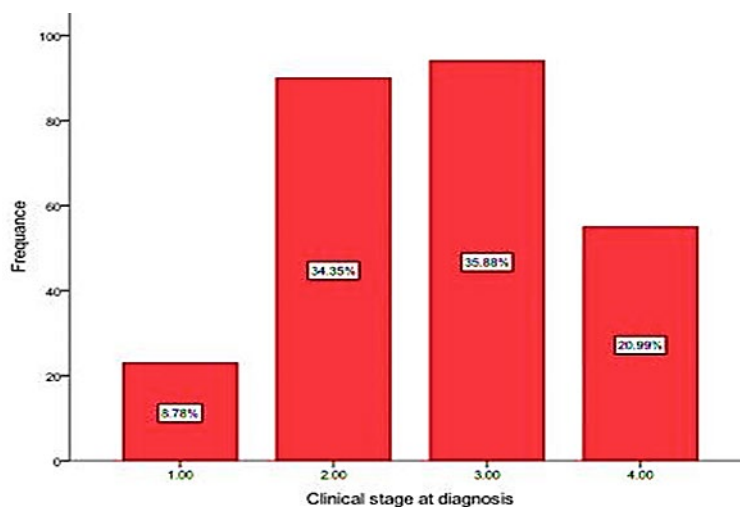


Figure (4). Stage distributions at diagnosis in 262 Libyan breast cancer patients (2013-2014).

Table (2). Clinical staging and TNM classification at the diagnosis in 262 Libyan breast cancer patients 2013-2014

	Tumor characteristics	No. of patients	Percentage %
Clinical stages	Stage 1	23	8.8
	Stage 2	90	34.4
	Stage 3	94	35.9
	Stage 4	55	21
Clinical stages	Early (1 and 2)	113	43.1
	Late (3 and 4)	149	56.9
T	T1	31	11.8
	T2	85	32.4
	T3	108	41.2
	T4	38	14.5
N 2.7	N0	67	25.6
	N1	99	37.8
	N2	76	29
	N3	20	7.6
M	M0	207	79
	M1	55	21

Diagnosis delay and associated factors: Delays in diagnosis were predicted by several factors: Of the patients, 139 (53.1%) did not consider their symptoms serious. In 9.2% of the patients, alternative therapy was used. For 9.2% and 0.8% of the patients, respectively, fear and shame kept them from seeing a doctor. After their initial visit to the doctor, 5 patients (1.9%) were not appropriately reassured that the lump was benign. Early breast symptoms in the absence of a lump were significantly linked to delayed diagnosis ($p < 0.0001$). Figure 5 displays the distribution of symptoms according to the diagnosis time (months). Women who did not report monthly breast self-examination tended to have longer diagnosis delays ($p = 0.002$). Before presenting their symptoms to a doctor, older women waited longer than younger women ($p > 0.0001$). Additionally, women who had taken oral contraceptives for more than five years ($p = 0.001$) and those who were illiterate ($p > 0.0001$) had a significantly higher risk of delay. Table 3 displays the diagnosis delay and related variables.

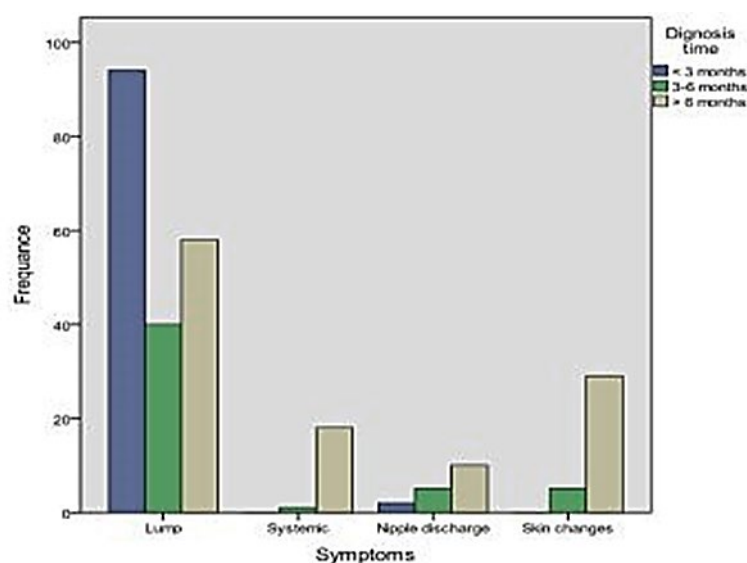
**Figure: (5).** Symptoms distribution according to diagnosis time (months) in 262 Libyan breast cancer patients (2013-2014).

Table: (3). Diagnosis delay in Libyan breast cancer in relation to socio-economic factors, health behaviors, and tumor-related factors

Predicting factors		Proportion of patients according to diagnosis time (percent)				P -value
		No. of patients	<3 months	3-6	>6months	
Age (years)	<50	170	45.3	17.6	37.1	<0.0001
	≥50	92	20.7	22.8	56.5	
Education	Literate	166	32.6	19.8	47.7	0.140
	Illiterate	96	44.4	18.9	36.7	
Occupation	Housewife	172	53	13.9	33.1	<0.0001
	Employed	90	8.3	29.2	62.5	
Marital status	Married	199	45.2	17.9	36.9	<0.0001
	Single	63	21.3	22.3	56.4	
Menopausal status	Pre-menopausal	168	35.7	17.6	46.7	0.199
	Post-menopausal	94	39.7	25.4	34.9	
Breastfeeding	Yes	160	38.8	16.9	44.4	0.251
	No	39	25.6	20.5	53.8	
Oral contraceptive	Yes <5 years	36	36.1	11.1	52.8	0.001
	Yes > 5 years	37	8.1	29.7	62.2	
Breast self Examination	No	189	42.3	19	38.6	0.027
	Yes	7	54.8	4.9	33.3	
Family history	Positive	255	33.2	20.9	45.9	0.021
	Negative	42	60	25	15	
History of benign breast disease	Yes	220	34.7	19	48.3	0.002
	No	20	100	0	0	
Symptoms	lump	242	34.9	20	45.1	<0.0001
	Others	192	49	20.8	30.2	
		70	2.9	15.7	81.4	

Association between diagnosis delay and clinical staging

Table 3 shows that 56.9% of patients had a late clinical stage of breast cancer. This stage was found in more women who had a diagnosis delay of more than six months (76.5%) than in those who had received a diagnosis less than three months after the onset of symptoms (1.3%; $p < 0.0001$). There was a significant correlation between large tumor size (T3 and T4; $p < 0.0001$) and positive lymph nodes (N2, N3; $P < 0.0001$) and diagnosis delay.

Out of the 55 patients who had metastases at the time of diagnosis, 96.4% had a diagnosis delay of more than six months ($p < 0.0001$) following symptoms. Table 4 displays the clinical stages of breast cancer at the time of diagnosis along with the associated diagnosis delay.

Table (4). Diagnosis delay and risk of late-stage breast cancer at the time of diagnosis

Tumor characteristics			Proportion of patients according to diagnosis time (percent)			
		No. of patients	<3 months	3-6	>6months	P -value
Clinical stages	Stage 1	23	100	0	0	<0.0001
	Stage 2	90	78.9	20	1.1	
	Stage 3	94	2.1	33	64.9	
	Stage 4	55	0	3.6	96.4	
Clinical stages	Early (1 and 2)	113	83.8	15.9	0.9	<0.0001
	Late (3 and 4)	149	1.3	22.1	76.5	
T	T1	31	90.3	9.7	0	<0.0001
	T2	85	70.6	17.6	11.8	
	T3	108	7.4	25	67.6	
	T4	38	0	15.8	84.2	
N 2.7	NO	67	97	3	0	<0.0001
	N1	99	29.3	22.2	48.5	
	N2	76	2.6	32.9	64.5	
	N3	20	0	10	90	
M	M0	207	46.4	23.7	30	<0.0001
	M1	55	0	3.6	96.4	

DISCUSSION

The most common and deadly tumor in women in Libya is breast cancer. Patients with breast cancer frequently have advanced stages at diagnosis, experience early disease recurrence, and have high death rates (Boder, J. et al. 2011). The majority of research in the developed world indicates that a delay of more than three months (total delay) between the onset of symptoms and the initiation of treatment is associated with an advanced clinical stage of breast cancer (El Mistiri, M. et al. 2007). Furthermore, there is a correlation between decreased survival and delays longer than three months.

(Ferlay, J. et al. 2012). Investigating diagnosis delay and comprehending its causes is essential to cut down on delays and enhance early diagnosis since delays are avoidable and have a significant impact on a patient's prognosis and outcomes. This study demonstrates that a major issue in Libya is the delay in breast cancer diagnosis. The length of time it took on average to receive medical advice and a diagnosis was greater than it was in developed or developing nations (Goodson, W. et al. 2002). This study reported several factors that are predictive of delayed diagnosis, which is consistent with other studies (Green, M. et al. 2008; Grunfeld, E et al. 2003). An important predictor of delay was the association between the patient-associated factors (psychology and/or sociology) and the delayed presentation of symptoms. According to some research, delays may have occurred when patients believed their symptoms would go away on their own without the need for medical

intervention (Najjar, H. et al. 2010). We discovered that many patients thought their symptoms were harmless and would go away on their own without the need for treatment. This was the main justification for delaying consulting a physician. The majority of patients sought out non-surgical treatments to avoid surgery. Certain patients held the belief that conventional medicines are more efficacious than contemporary medications, or that there are no effective treatments available for breast cancer. The majority of patients reported worsening symptoms while on alternative treatments, which ultimately resulted in a more advanced stage. Compared to 41.5% in other studies, 9.2% of respondents in this study reported using alternative therapies rather than going to the doctor (Jones, R. et al. 2007).

This study demonstrated that delays were caused by unfavorable information regarding breast cancer diagnosis and treatment. Some patients thought there was no use in getting diagnosed and treated for breast cancer because it could not be cured (Keen, J. et al. 2009). Some women may choose not to get their symptoms checked out if they suspect breast cancer because they are afraid of their husbands divorcing them or getting remarried. Negative information about chemotherapy's side effects and anticipated toxicity caused patients to become afraid of the treatment and refuse it. Delays in diagnosis were also linked to the perception that mastectomy results in disability and disfigurement (Montella, M. et al. 2001). Moreover, stigma and the individual desire to conceal symptoms were factors contributing to the delay in diagnosis, especially for older women in this study who were over 50. There are some "alarm symptoms," significant prediction of cancer diagnosis. But nurses and physicians don't always know about these. Even though the majority of lumps in young patients are benign, doctors should encourage diagnostic tissue sampling from all palpable breast masses as a simple way to avoid delays in diagnosis. In this study, respondents were unnecessarily reassured that a lump could be deemed benign without a biopsy following the initial visit. This mindset is untrue and played a significant role in the length of the diagnosis period in this investigation. Remarkable outcomes were documented by (Nadia, M. et al. 2007).

One of the study's key findings demonstrated a strong correlation between the early symptoms of breast cancer (which did not include a lump) and the delay in receiving a diagnosis. According to other studies, finding a breast lump shortens the time patients must wait. The findings imply that education regarding the various forms of breast cancer symptoms is necessary for both physicians and patients. According to this study, patients who performed monthly self-examinations were younger, more educated, and requested medical assistance more quickly than older or less educated patients. Although clinical breast examination (CBE) and breast self-examination (BSE) can both improve the diagnosis of breast cancer without incurring the costs of a mammography facility, mammography remains a sensitive method for early detection of breast cancer (Neal, R. et al. 2008). Additionally, this study found that older women delayed seeing a doctor about their symptoms longer than younger women. Numerous studies have found that receiving a diagnosis later in life is correlated with older age. As such, any intervention program addressing this issue should focus on older women. Numerous studies have reported on the impact of education on symptoms of breast cancer (Norsa'adah, B. et al. 2011).

This work highlights the significant issue of breast cancer ignorance in Libya. Public education campaigns are necessary, particularly for women with lower levels of education. A higher likelihood of delayed diagnosis was seen in women with a history of fibrocystic disease. The explanation is that if previously benign breast tissue alterations are still deemed benign by medical professionals. Therefore, it might be beneficial to advise women who have a known benign breast disease to report any new breast symptoms as soon as possible. Doctors should also be aware that any new symptoms should be considered as possible risks for breast cancer. According to this work, there is

a significant impact of diagnosis delay on the disease's stage and potentially on survival. Additionally, there was a significant correlation between lymph node involvement and diagnosis delay, greater tumor size, a high rate of metastatic disease, and advanced clinical stages. 59.9% of Libyan patients waited more than three months to seek medical advice, with a median consultation duration of 120 days. Just 18% of patients in Europe waited longer than three months before seeking medical advice, with a median consultation duration of 16 days. However, 56.9% of Libyan patients presented with an advanced stage, with a mean age of 47.8 years. In contrast, 57.5 years was the average age of patients in Europe, and 51% were in a late stage. The variations in these outcomes could be due to variations in healthcare or other patient-related, societal, and/or demographic factors. Additionally, compared to European women, Libyan women with breast cancer appear to have a lower mean age and a more advanced stage at the time of diagnosis.

The discovery that patients in Libya have a low mean age at diagnosis, indicating that premenopausal cancers are more common than in Europe, is one of the study's key findings. These also support findings from other Libyan studies (Richards, M. et al. 1999). The age distribution of breast cancer patients in Africa or the Middle and North Africa (MENA) region is consistent with this age distribution (Stapleton, J. et al. 2011). These findings imply that premenopausal type predominates among breast cancer patients from Libya and other African countries. When diagnosed with breast cancer, the majority of patients in the US and Europe are postmenopausal. According to our research, patients in Libya typically present with an advanced stage, an early disease recurrence, and a possible high mortality rate. Our results support other earlier findings regarding the high proportion of patients in advanced stages. As observed in this study, the study on breast cancer in Nigeria (Velikova, G. et al. 2004), and other studies conducted in North African countries, suggest delayed presentation and late diagnosis. This trend may be explained by women's low health awareness, ineffective information campaigns, and Libya's lack of mammography or other screening programs for early breast cancer detection. Although mammography is not included in Libya's screening program, its potential is possibly limited due to the challenges associated with achieving an early mammographic diagnosis of premenopausal breast cancer (Weiss, N. et al. 2003).

CONCLUSION

In Libya, delayed diagnosis is a major issue. Delays in diagnosis have been linked to intricate interactions between medical, social, and other patient-related factors that progress symptoms and may increase mortality. In order to promote early detection, it is necessary to raise public awareness of breast cancer and establish screening facilities.

ETHICS

The study was approved by the Research Ethics Board (REB) at Benghazi Medical Center (BMC) before its commencement.

Duality of interest: The authors declare that they have no duality of interest associated with this manuscript.

Author contributions: A.B. developed the theoretical formalism, performed the analytic calculations, and performed the numerical simulations. Both A.B. and B.C. authors contributed to the final version of the manuscript. B.C. supervised the project.

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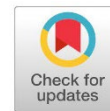
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Research Article

6 Open Access



Study of Bacterial Contamination in the Operating Room and Newborn Intensive Care Unit: Effects of the Predominantly Used Antibiotics at Sabratha Teaching Hospital

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Abstract

Contamination by bacteria in the operating room (OR) and newborn intensive care units (NICU) has continued to increase the incidence of nosocomial infections and a center point of multidrug-resistant (MDR) pathogens. This study was to examine the spread of bacteria isolated from inanimate surfaces in the operating room and neonatal intensive care units at Sabratha Teaching Hospital and find out the effectiveness of the most antimicrobial used. Methods: At the Sabratha Teaching Hospital in Sabratha, Libya, a cross-sectional, descriptive study was conducted in the OR and NICU from February to May 2024. A total of 22 swab samples were collected from high-contact environmental surfaces. Isolation, identification, and antibiotic sensitivity patterns were performed via standard techniques. Results: After 48 hours of incubation, (54.5 %) of the swabbed surfaces showed positive bacterial growth and 45.5% showed no bacterial growth, of which 25% had gram-positive bacteria and 75% had gram-negative bacteria. *Staphylococcus saprophyticus* 3 (25%) was the identified gram-positive bacterial isolate, and *Klebsiella* spp. 5 (55.5%) and *Pseudomonas aeruginosa* 4 (44.4%) were the probable gram-negative bacterial isolates. The antimicrobial susceptibility pattern of clinical pathogens tested *Staphylococcus epidermidis* and *Klebsiella* spp showed similar patterns which were sensitive to most antimicrobials used, while *Pseudomonas aeruginosa* was highly resistant to Cotrimoxazole, Cefatoxime, Cefixitin, Ceftazidime, Ceftrixillin, and Calvu amoxicillin. Conclusion: This study confirms the need for rigorous disinfection protocols and hand hygiene to reduce the spread of these pathogens in the OR and NICU.

Keywords: Antibiotic Resistance, Intensive Care Unit, Nosocomial Infection, Operating Room, *Staphylococcus Epidermidis*.

INTRODUCTION

Patients treated at a hospital or other healthcare institution but not present at the time of admission may contract nosocomial infections, sometimes known as "hospital-associated infections" (HAIs). These conditions may arise while treating other conditions or after the patient is released from the hospital. It also covers illnesses that employees contract at work (Haque *et al.* 2018). In rich nations, seven out of every 100 hospitalized patients may have one of these infections linked to healthcare, while ten out of every 100 patients in impoverished nations may have one (Haque *et al.* 2020).



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Bacteria may cause injury to patients in operating rooms (ORs) and heavily taxed hospitals (Weinstein 1998). Depending on the quantity of bacterial pathogens present, various sources have different effects on the degree of bacterial contamination. Similarly, the degree of contamination can be decreased if hospital staff members pay attention to hygiene standards and a hospital's environment, particularly, its cleanliness and disinfection are the primary factors in lowering the danger of microbial infection (Mora and Alanta 2001). The breathing pattern in active operating rooms and intensive care also helps reduce infection levels (Okon *et al* 2012). Hospitals are reservoirs of different types of microbes; many pathogenic bacterial species have colonized frequently touched areas (Shiferaw *et al.* 2013). Infectious mechanisms, high antibiotic use, and patient-to-patient bacterial transmission due to inadequate infection control measures may explain why operating rooms and intensive care units are "hot zones" for the presence and spread of microbial resistance (Bhalla *et al.* 2007). The impact of bacterial contamination on operating rooms and hospital care and its overall impact on hospital infection control is important for the patient and the healthcare team (Tacconelli *et al.* 2018, Rochford *et al.* 2018).

A significant public health issue that contributes to higher rates of morbidity and mortality as well as longer hospital stays is the morbidity associated with infections in newborn care. According to published research, the infection frequency linked to healthcare in newborn intensive care units (NICUs) varies from 8.7% to 74.3% (Kajiyazdi *et al.* 2021, Chiguer *et al.* 2019, Cura *et al.* 2016).

The neonatal period, which lasts for four weeks and accounts for approximately 3.6 million deaths annually, is primarily caused by infections, complications from premature birth, and intrapartum-related neonatal deaths (birth asphyxia) (Lawn *et al.* 2010). Because of the severity of their illness and their exposure to medical devices such as central venous catheters (CVCs) and mechanical ventilators, as well as resistant microorganisms, newborns admitted to intensive care units (ICUs) are quite dangerous for nosocomial infections (NI) (Chiguer *et al.* 2019). The types of organisms that cause infections vary geographically and over time, and the emergence of antibiotic-resistant organisms has become a major global health concern (Ingale *et al.* 2017).

There is a link between the presence of pathogens on hospital surfaces and equipment and the frequency with which they are cleaned, how they are cleaned, appropriate use of disinfectants, and appropriate decontamination. Gram-negative and Gram-positive bacteria have been isolated from inanimate surfaces and can survive persistently for months on dry surfaces at humid and lower temperatures (Sales *et al.* 2014).

The rate of contamination in operating rooms and critical care units is influenced by numerous factors. These include the inoculum size, moisture content, source and target surface, and organism species. The setting of the critical care unit, the number of nurses, the number of patients colonized or infected, and hand hygiene compliance are other significant factors (D'Alessandro *et al.* 2021).

These infections are more serious and cause more deaths in intensive care if caused by resistant bacteria, especially infections from venous catheters or ventilator infections. Nosocomial infections are caused by various reasons, including hospital staff and ventilation and breathing systems. Treatment for bacterial infections is typically individualized and based on the patient's clinical picture. Consequently, it's essential to identify every strain of the bacteria that could be causing nosocomial infections. More antibiotics are advocated when information on bacterial occurrence in the critical care unit and operating room is lacking and their antimicrobial resistance is unclear. This can result in the improper use of antibiotics. It not only provides no

treatment benefits but also creates problems for patients. The misuse of antibiotics is known to cause *Clostridium difficile* bacteria, which causes diarrhea. Understanding the mechanisms of bacterial incidence and drug resistance in the intensive care unit and operating room is considered the first step in treating infectious diseases (Bobo and Dubberke 2010, Esfahani *et al.* 2017). Although the number of beds in intensive care units is low, the number of hospital-acquired infections is high. Nowadays, controlling the risk of nosocomial infection is becoming a priority (Merzougui, *et al* 2018). Since infectious diseases are transmitted from patients in intensive care and account for almost half of all infections, controlling and reducing the spread of infectious diseases in these regions provides significant economic benefits.

In relation to the above introduction, this study aimed to investigate abiotic surface infections in the newborn intensive care unit (NICU) and operating room (OR) to evaluate the effectiveness of the most commonly used antibiotics.

MATERIALS AND METHODS

Study design and setting

This cross-sectional study was conducted from February to May 2024 in the operating room and newborn intensive care unit (NICU) of the Sabratha Teaching Hospital in Sabratha, Libya.

For this study, 22 swab samples were taken from high-contact surfaces, including [gowns, instrument boxes, tables of instruments before operations, bedside, reception desks, liquid soap, betadine, incubator sides, neonatal beds, suction tips, ventilators, ambu bags, digital weighing machines, waterpots, and staff tables].

Sample collection

Sterilized cotton swabs were labeled, collected, and placed in a tube containing nutritional broth an hour after the samples were obtained. The swabs were inoculated onto nutrient agar in the lab and kept overnight at 37°C. MacConkey agar was used for subculture, and blood agar plates were purified by aerobic 24-hour incubation at 37 °C.

Identification of Isolated Bacteria

Standard microbiological methods, such as colony morphology, and Gram stain are used to differentiate between Gram-positive and Gram-negative bacterial isolates. Comprehensive biochemical analyses using oxidase, coagulase, and catalase were performed to determine all pure isolates (Cheesbrough, 2009).

Antibiotic susceptibility of the isolated bacteria

The Clinical and Laboratory Standards Institute (CLSI) guideline (Yusuf *et al.* 2017) states that modified Kirby-Bauer disk diffusion is employed for antibiotic susceptibility testing following isolation and identification. The standard medium for the Kirby-Bauer method of susceptibility testing is Muller Hinton Agar (MHA). A filter paper tablet containing a known concentration of the antibiotic in a precise amount is used to calculate the minimum inhibition concentration (MIC). (Weinstein *et al.* 2018). One pure colony of bacteria was combined with one drop of sterile normal saline to create the bacterial suspension. The bacterial suspension was then compared to the McFarland standard to identify the concentration of the bacteria.

The test organism suspension was swabbed across the whole area of the MHA plate. After rotating the platter 360 degrees and doing so three times, let the dishes air dry fully. Using tongs, after adding the antibiotic tablets to the contaminated plates, the dishes were incubated for one whole day at 37°C. To evaluate the isolates' susceptibility to different antibiotics, inhibition regions were also measured around each antibiotic tablet using the provided ruler. Some areas around the disc showed no microbial growth, indicating that the antibacterial agent is effective; Microbes were growing

around the disc in other regions, suggesting that there was no zone encircling it and that the antibacterial chemical was inert.

In this study, antibiotic disks used were Cotrimoxazole 0.75 mg (COT 0.75), Amikacin 1 mg (AMK 1), Cefatoxime 1mg (CTX 1), Cefoxitin 1 mg (FOX 10), ciprofloxacin 5 mg (CIP 5), Ceftazidime 1 mg (CAZ 1), imipenem 10 mg (IMI 10), Polymixin 30 mg (POL 30), Linezolid 3 mg (LNZ 3), Meropenem 1mg (MER1), Ceftricillin 3 mg (CTR 3), Clavu amoxicillin 1 (AUG 1), Gentamycin 1mg (GEN 1), manufactured by the Bioanalyse company.

RESULTS

After 48 hours of incubation, 12 samples (54.5%) out of the 22 swabs that were analyzed for the presence or absence of bacteria exhibited evidence of growth, while the other 10 samples (45.4%) showed no growth.

Additionally, the findings demonstrated that 9 samples (75%) contained Gram-negative bacteria and 3 samples (25%) included Gram-positive bacteria. The potential Gram-positive organism isolated was *Staphylococcus epidermides* 3 (100%). The majority of *Staphylococcus epidermides* in the operating room have been isolated from the staff table, operating bed, and reception table. The potential Gram-negative organisms isolated were *Pseudomonas aureuginosa* 4 (44.47) and 5 (55.5%) *Klebsiella* spp isolates from the suction tip, liquid soap, baby incubator heater 3, neonate bed, and ambu bag. *Pseudomonas aeruginosa* isolates, however, were recovered from the suction tip, operation bed, outside surface of the incubator, and the water of the baby incubator 3.

Table (1). The Types and frequency of bacteria isolated from inanimate surfaces in the operating room and neonatal intensive care unit at Sabratha Teaching Hospital

Type of isolates	Gram-positive (n=3)	Gram-negative (n=9)
	3(25%)	9(75%)
	Gram-positive isolates	Percentage
	Frequency	
<i>Staphylococcus epidermides</i>	3	25%
	Gram-negative isolates	
<i>Klebsiella</i> spp	5	55.5%
<i>Pseudomonas aeruginosa</i>	4	44.47%

The isolated bacteria's antibiotic susceptibility tests, as indicated in Tables 2, 3, and 4, revealed an even pattern with a high level of resistance to Cotrimoxazole, Cefatoxime, Cefixitin, Ceftazidime, Ceftricillin, Ceftricillin, and Clavu amoxicillin.

Table (2). The antibiotic sensitivity profile of *Staphylococcus epidermides*

organism	Antimicrobial	Total tested	Sensitive n(%)	Intermediate n(%)	Resistance n(%)
<i>Staphylococcus epidermides</i>	Cotrimoxazole	3	3(100%)	0 (0%)	0(0%)
	Cefatoxime	3	3(100%)	0(0%)	0(0%)
	Ciprifloxacin	3	3(100%)	0(0%)	0(0%)
	Polymixin	3	3(100%)	0(0%)	0(0%)
	Linezolid	3	3(100%)	0(0%)	0(0%)
	Vancomycin	3	3(100%)	0(0%)	0(0%)
	Ceftricillin	3	0(0%)	3(100%)	0(0%)

Although the isolates were too few to provide meaningful antimicrobial sensitivity analysis, the organism (*Staphylococcus epidermides*) had intermediate resistance to cefticillin but was sensitive to all other antimicrobials.

Table 3: The antibiotic sensitivity profile of *Klebsiella* species

Organism	Antimicrobial	Total tested	Sensitive n(%)	Intermediate n(%)	Resistance n(%)
<i>Klebsiella</i> spp	Cotrimoxazole	5	5(100%)	0 (0%)	0(0%)
	Cefatoxime	5	5(100%)	0(0%)	0(0%)
	Cefoxitin	5	5(100%)	0(0%)	0(0%)
	Ceftazidime	5	5(100%)	0(0%)	0(0%)
	Polymixin	5	5(100%)	0(0%)	0(0%)
	Gentamycin	5	5(100%)	0(0%)	0(0%)
	Clavu amoxycillin	5	5(100%)	0(0%)	0(100%)

Although the isolates were too few to provide a meaningful antimicrobial sensitivity, the organism (*Klebsiella* spp) was sensitive to all the antimicrobials.

Table 4: The antibiotic sensitivity profile of *Pseudomonas aeruginosa*

Organism	Antimicrobial	Total tested	Sensitive n(%)	Intermediate n (%)	Resistance n(%)
<i>Pseudomonas aeruginosa</i>	Cotrimoxazole	4	0(0%)	0 (0%)	4(100%)
	Amikacin	4	4(100%)	0(0%)	0(0%)
	Cefatoxime	4	0(0%)	0(0%)	4(100%)
	Cefixitin	4	0(0%)	0(0%)	4(100%)
	Ciprofloxacin	4	4(100%)	0(0%)	0(0%)
	Ceftazidime	4	0(0%)	0(0%)	4(0%)
	Meropenem	4	4(100%)	0(0%)	0(100%)
	Cefticillin	4	0(0%)	0(0%)	4(100%)
	Clavu amoxicillin	4	0(0%)	0(0%)	4(100%)

Pseudomonas aeruginosa showed a high degree of resistance to Cotrimoxazole 4 (100%), Cefatoxime 4 (100%), Cefixitin 4(100%), Cefticillin 4(100%), and Clavu amoxicillin 4(100%). Among *P. aeruginosa*, 100% sensitivity was observed with Amikacin, Ciprofloxacin, Ceftazidime and Meropenem.

DISCUSSION

Recent studies have shown that microbial contamination of the OT and ICU environment can lead to colonization and infection of patients. Due to their weakened immune systems from invasive medical operations during their hospital stay, patients in intensive care units are most vulnerable to hospital-acquired infections or HAIs. Physicians and intensive care unit staff may act as carriers for the transfer of infectious diseases from other hospitals to the intensive care unit. Therefore, the hands of ICU staff and healthcare workers (HCWs) must follow the tightest hygiene guidelines. Furthermore, the ICU environment's pollution greatly contributes to nosocomial illness acquisition in both patients and healthcare workers. Examining the frequency of bacterial contamination on healthcare workers' hands and the surfaces in the intensive care unit could yield suggestions for limiting the spread of dangerous bacteria to patients and staff in medical environments (Tajeddin *et al.* 2016).

Hazardous infections could arise from contaminated healthcare workers' contact with hospitalized patients in intensive care units. The presence of live bacteria in the squamous layer of skin, which is constantly shed from healthy skin, is the reason behind the contamination of bed linens, patient robes, and other items in the intensive care unit (Tajeddin *et al.* 2016). One of the main causes of the increased rates of nosocomial infections in NICUs is bacterial contamination. During the care of diseases, non-critical medical equipment and inanimate surfaces may contain bacteria for an extended period and come into touch with patients and medical staff (Darge *et al.* 2019, Nseir *et al.* 2011). On dry surfaces, the majority of gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA), can persist for months (From seven days to seven months). Numerous Gram-negative bacteria, including *Klebsiella* species, *E. coli*, and *Acinetobacter* species, on dry surfaces, can survive for up to 30 months (Suleyman *et al.* 2018).

According to our findings, a wide range of bacteria including, Gram-positive (25%) and Gram-negative (75%) bacteria, were present on non-living surfaces. In contrast to research done in Zimbabwe in tertiary hospitals in Bulawayo's intensive care units, Gram-negative bacteria (66.18%) constituted the majority of bacterial isolates (33.82%) as opposed to Gram-positive bacteria (Mbanga *et al.* 2018). This study is comparable to one carried out in the NICU of the Manipal Teaching Hospital in Pokhara, Nepal, where the majority of bacterial isolates were Gram-negative (66.3%) as opposed to Gram-positive (33.6%) (Bhatta DR. 2021).

The findings of this study differ from those of one conducted in the obstetrics and gynecology department of Al-Jala Hospital in Tripoli, Libya, where a higher proportion of bacterial isolates (68.9%) were Gram-positive than Gram-negative (31.03%) (Ben Ashur *et al.* 2022). This could be the result of sampling from various surfaces; it could also be the result of sporadic disinfection, variations in the disinfectant kinds used, unhygienic conditions, and crowding.

This study's overall bacterial contamination rate of (54.5%) is comparable to a study conducted at Windhoek Central Hospital in Windhoek, Namibia, where the neonatal intensive care unit (NICU) showed contamination rates of (52.8%) (Alphons *et al.* 2020). The study's (52.8%) contamination rate is consistent with findings from another study conducted at the intensive care section of a tertiary hospital in Bauchi, northeastern Nigeria, which recorded (52.8%) contamination rates for neonates (Alphons *et al.* 2020).

An investigation conducted in the tertiary hospital in Bulawayo, intensive care units, Zimbabwe, revealed a significantly greater contamination incidence of 86.1% (Mbanga *et al.* 2018). The contamination rate in this study is also much lower when compared to a study done in Morocco and Libya which reported a contamination rate of 96.3% and 95% respectively (Ben Ashur *et al.* 2022, Lalami *et al.* 2016). The high contamination rate recorded in NICU in this study and other similar studies around the globe is caused by several factors, including the large number of newborns who are often admitted for clinical care and assessment and have a variety of clinical problems. The constant presence and attention of nursing mothers and healthcare professionals is necessary for this therapeutic practice, which raises the intensity of human activity, mobility, and unit occupancy (Yusuf *et al.* 2017).

Variations in hand hygiene and sterilization procedures in neonatal intensive care units could account for the differences. In this study, the most common bacterial contaminants shown in (Table 1) were *Klebsiella* spp which accounted for (55.5%) of all isolates, followed by *Pseudomonas aeruginosa* which accounted for (44.4%) and *Staphylococcus epidermides* contributed (25%). These results align with the findings of a study in Benghazi, Libya, where *Klebsiella*. Spp and *Pseudomonas aeruginosa* were the most prevalent isolates. Other studies showed that *Klebsiella* spp and *Pseudo-*

monas aeruginosa bacteria were the most prevalent in such areas (Ensayef *et al.* 2009, Tajeddin *et al.* 2016).

The OR and NICU surfaces' microbial flora do not differ significantly from those of other hospital environments. Furthermore, preventing nosocomial infections in the NICU is made more difficult by the high susceptibility of premature and immunocompromised neonates. Colonization of NICU surfaces by opportunistic nosocomial pathogens like *Klebsiella* spp, *Staphylococcus epidermides*, and *Pseudomonas aeruginosa* are important for high-risk hospitalized patients like nosocomial infection. Additionally, there are significant dangers for babies, including low birth weight and congenital and neonatal defects.

In antimicrobial susceptibility profiles, *Staphylococcus epidermides* in this study (as seen in Table 2) showed high sensitivity to Cotrimoxazole (100%), Cefatoxime (100%), ciprofloxacin (100%), Polymixin (100%), Linezolid (100%), and Vancomycin (100%), but it was intermediate sensitive to Ceftracillin (100%). In another study, there is a difference in *Staphylococcus epidermides* sensitivity, which was moderately sensitive against gentamycin (71.4%), tetracycline (71.4%), clindamycin (50.0%) and Ciprofloxacin (42.9%). A low sensitivity against erythromycin (14.3%), with an intermediate resistance of (14.2%) was noted. These microorganisms were highly resistant to cefoxitin (100%) and penicillin (100%) (Alphons *et al.* 2020). These results were similar to those found in a study done in Nigeria where 90%, 100%, and 100% sensitivity was reported against ciprofloxacin, gentamycin, and erythromycin respectively (Yusuf *et al.* 2017).

In this study (as shown in Table 3) *Klebsiella* species showed a high sensitivity to Cotrimoxazole (100%), Cefatoxime (100%), Cefoxitin (100%), Ceftazidime (100%), Polymixin (100%), Gentamycin (100%), and Clavu amoxicillin (100%).

The result obtained in this study (as reported in Table 4) for the antimicrobial susceptibility patterns of *Pseudomonas aeruginosa* showed high sensitivity to Amikacin (100%), ciprofloxacin (100%), and meropenem (100%). But it was resistant to Cotrimoxazole (100%), Cefatoxime (100%), Cefixitin (100%), Ceftazidime (100%), and Clavu amoxicillin (100%). These results were similar to a previous study done in Windhoek which reported a high sensitivity to cefepime (100%), ciprofloxacin (100%), piperacillin-tazobactam (100%), and meropenem (100%). It was also resistant to gentamycin, ceftazidime, and imipenem (Alphons *et al.* 2020). Similar findings were also reported in a study done in Iran, which showed high resistance to Gentamycin (79%), Ceftazidime (25%), and Amikacin (83%) (Ekrami *et al.* 2011). These results were not consistent with the results of a study done in Bulawayo, Zimbabwe, in which high resistance to Gentamycin (62.5%), Piperacillin-tazobactam (50%), and Amikacin (12.5%) was reported (Mbunga *et al.* 2018).

CONCLUSION

One of the most important complications of hospitalized patients in OR and neonates is nosocomial infection in the NICU where contamination rates are very high. In the NICU and OR, (54.5%) of non-living surfaces and equipment were contaminated with germs. The isolation of pathogenic bacteria in this study such as *Staphylococcus epidermides* and *Klebsiella* spp indicate that they can be vehicles for disease transmission. Because of this, the operating room and neonatal intensive care unit where patient interaction with healthcare workers (HCWs), parents, and relatives is frequent and common, need rigorous disinfection and careful contact control procedures to reduce the spread of these pathogens.

Various interventions are required for the best possible infection control in the complex ecosystem, that is, the hospital setting. The most significant issues in hospital settings include the lack of a

standard protocol for nosocomial infection surveillance, high levels of bacterial contamination on hospital environmental surfaces, and poor hand hygiene.

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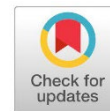
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Research Article

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Epidemiological Criteria and Management of Pediatric Inpatients with Community-acquired Pneumonia at Tobruk Medical Center - Libya

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Abstract

The clinical manifestations of pneumonia obtained outside of a hospital setting are known as community-acquired pneumonia (CAP). Pneumonia is the most frequent infectious cause of child mortality worldwide. This study aims to evaluate the epidemiological criteria of community-acquired pneumonia in pediatric inpatients from 29 days to under 18 years, as well as the management and consequences of the condition. Data from the admission records of 365 patients with CAP, ages 29 days to under 18 years old, were gathered for the retrospective study, these patients made up 15.9% of hospital admissions. The M/F ratio was 1.2:1, with 198 (54.2%) male patients, predominantly infants, 221 (60.5%) ($p < 0.001$), and mostly came from Tobruk 311 (85.2%). Most cases were in Winter 170 (46.6%). Patients admitted to the intensive care unit had longer hospital stays 3.5 days on average. There were no deaths among the patients, and of those who required an intensive care unit (84 patients, 23%), 30 patients required an oxygen supply by using a nasal cannula and without the requirement for mechanical ventilation. The most often given intravenous antibiotic in 291 cases (79.7%) was cefotaxim (Claforan), whereas penicillin was used in 173 cases (47.4%). We conclude that Infants were the predominant age group that developed CAP and required PICU admission, with a higher incidence throughout the winter months.

Keywords: Community-Acquired Pneumonia, Epidemiological Criteria, Tobruk Medical Center-Libya.

INTRODUCTION

Both bacteria and viruses can cause pneumonia, an infection of the alveoli and distal bronchi in the lower respiratory tract. Clinical manifestations of pneumonia gained outside a hospital setting are explicitly referred to as community-acquired pneumonia (CAP) (Harris M et al. 2011). The leading infectious cause of mortality for children globally is pneumonia. Pneumonia killed 740180 children in 2019 (WHO 2022). It is the leading cause of death for children under the age of five. Low- and middle-income nations account for most of these fatalities (Nair H et al., 2013). Childhood pneumonia was associated with a history of low birth weight, severe malnutrition, partial or nonexclusive breastfeeding, indoor air pollution, and incomplete basic vaccinations (Vivi Ninda et al. 2021). According to O'Brien KL et al. (2009) and Watt JP et al. (2009), the main organisms linked to



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childhood CAP include *Mycoplasma pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Chlamydia pneumoniae*, and *Streptococcus pneumoniae*. Numerous viral pathogens have also been identified as significant causes of community-acquired pneumonia (CAP), including influenza, rhinoviruses, human metapneumoviruses, adenoviruses, and respiratory syncytial virus (Jain S et al. 2015; Nair H et al. 2010). A combination of bacteria and viruses causes one-third of CAP cases. Generally, viruses cause 30–67% of pediatric CAP cases and are more common in children under the age of one than in those over the age of two (Harris M et al. 2011). Frequently, the diagnosis is determined based on clinical findings, such as fever, cough, breathing difficulty, nasal flare-ups, retractions of the intercostals, subcostals, and suprasternal, and grunting with or without X-ray signs of an acute lung infiltration or consolidation. (Messinger AI et al. 2017).

Tachypnoea seems to be the most relevant clinical indicator because it's linked to the overall severity of CAP, lung infiltrates on chest radiographs, and hypoxemia (Harris M. et al. 2011). Based on age-related reference values, the medical description of the condition is as follows: < two months of age, > 60 breaths/min; two months up to one year > 50/min; one year to five years, > 40/min; and more than 5 years, > 20/min (Bradley JS et al. 2011). The prevalence of bacterial pneumonia has declined since the development of protein conjugate vaccines against *Streptococcus pneumoniae* and *Haemophilus influenzae* (Kaplan et al. 2015; Morris et al. 2008). Cristiano Alicino et al. (2017) state that the pneumococcal conjugate vaccines, which are 10-valent and 13-valent, PCV 10 and PCV13, significantly lower hospitalization rates for pneumonia. This is especially true for children under 24 months of age. Even though the developed world has a far lower prevalence of CAP-related mortality than the developing world, CAP nevertheless, accounts for a sizable share of medical visits and hospital stays in high-income nations.

This study aims to evaluate the epidemiological criteria of community-acquired pneumonia in pediatric inpatients from the age of 29 days to under 18 years, as well as the management and consequences of the condition.

MATERIALS AND METHODS

By gathering information from the Statistics Office, a retrospective analysis was conducted. The patient admission files provided the source of the data. These are the details of the CAP patients from July 2022 to June 2023, ranging in age from 29 days to under 18 years. Included were the date of admission, date of discharge, patient's gender, age, nationality, place of residence, admission type (general pediatric ward or PICU), any family history of the same illness, treatment options, and mortality. The incidence of CAP in children between the ages of 29 days and under 18 was the primary outcome measure. The percentage of patients in three age groups 29 days to 1 year (Infants), > 1 year to 5 years (young children), and > 5 years to 18 years (School-aged children), the percentage of male and female patients, the percentage of patients admitted to the PICU, the management strategy, seasonal variation, and regional distribution were the secondary outcome measures.

Statistics Analysis

The statistical package for social scientists, version 25, and percentage-expressed data were used in the statistical study. P values below 0.05 were regarded as statistically significant.

RESULTS

Between July 2022 and June 2023, a total of 2296 patients were admitted to the Pediatric Ward; 381 had CAP, of which 16 were excluded due to their age being under 29 days. This means that 365 patients with CAP between 29 days and under 18 years old account for 15.9% of all hospital admis-

sions. With an M/F ratio of 1.2:1 and 198 (54.2%) of the patients were male, 85.2% of the total originated from Tobruk 311, with the remaining originating from the surrounding area.

Hospital admissions for CAP were significantly higher in the winter, peaking in December 59 (16.2%) and January 83 (22.7%). The variation in the season was as follows: Winter 170 (46.6%), Spring 58 (15.9%), Summer 70 (19.2%), and Autumn 67 (18.3%) (P-value = 0.04), Figure 1 illustrates this.

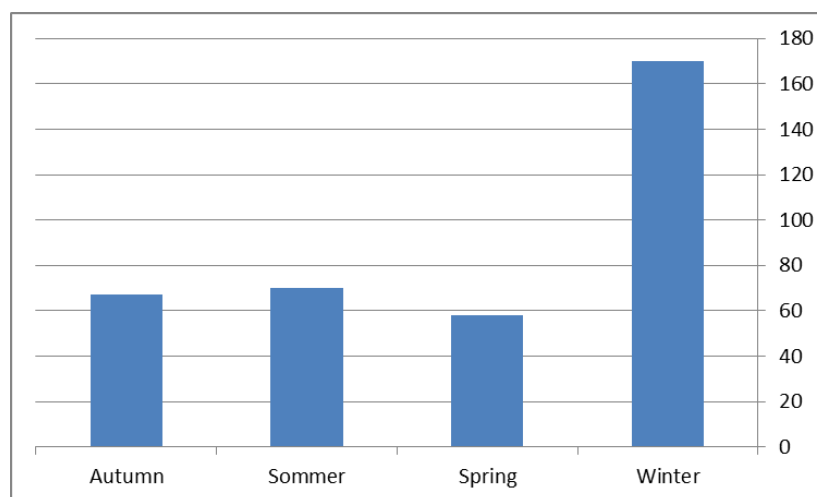


Figure: (1). Seasonal variation of CAP

The patients were 23.7 months old on average, divided into three age groups: 221 (60.5%) for Infants, 104 (28.5%) for young children, and 40 (11%) for School aged children (p value < 0.001), Figure 2 illustrates this.

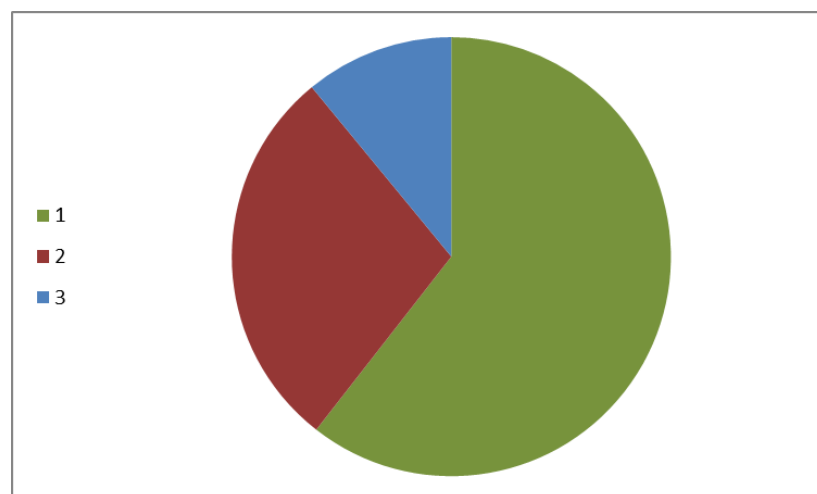


Figure: (2). Age Groups of patients: 1. Infants, 2. Young children, 3. School-aged children.

Thus, there was a significant increase in CAP in infants under one year old, particularly throughout the winter. 7 patients (1.9%) left against medical advice (LAMA). The mean duration of hospital stay was 3.5 days, with an increase in patients who needed PICU treatment. Among the 84 (23%), 30 (8.2%), needed an oxygen supply while they were in the PICU, and 61 (72.6%) of them were infants, Figure 3 illustrates this, no deaths were reported. Infants were the predominant age group that developed CAP and required PICU admission, with a higher incidence throughout the winter

months. Cefotaxim (Claforan) was the most often used intravenous antibiotic in 291(79.7%). Penicillin was used in 173 cases (47.4%), Macrolide in 33 cases (9%), Cefixime in 33 cases (9%), and small percentages of Ampicillin, Cloxacillin, Meropenem, and Amikacin were also utilized.

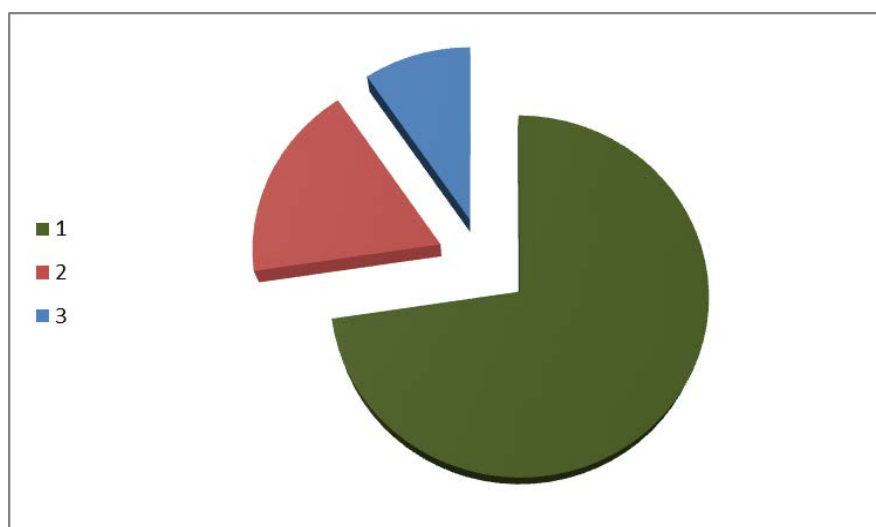


Figure: (3). PICU cases of CAP, 1= Infants, 2=Young Children, 3= School-aged children

DISCUSSION

During this study, we reported 365 hospitalizations for community-acquired pneumonia among children aged 29 days to under 18 years old, accounting for 15.9% of total hospital admissions during that period.

With an average age of 23.7 months, the majority of participants of the study were in the infant age range (> 29 days to 1 year), the same findings were found in studies conducted in Alexandria, Egypt (Noha Fadl et al., 2020), Iraq (Mortadha H Kreeb Al-Dalfi et al. 2023) and in Syria (Damascus) (Abdullah Almouslli et al. 2023). In our research, there are 198 (54.2%) more male patients than female patients (1.2:1), studies were carried out in Alexandria, Egypt (Noha Fadl et al., 2020), Syria (Damascus) (Abdullah Almouslli et al., 2023), Iraq (Mortadha H Kreeb Al-Dalfi et al. 2023) and southern Brazil (Tiago Neves Veras et al., 2011) which revealed similar results.

The study demonstrates a correlation between seasonal changes and the incidence of CAP; the findings, which were confirmed by an Australian study, indicate that the incidence was higher in Winter 170 (46.6%). (Katherine M Murdoch et al 2014).

Third-generation cephalosporins, especially cefotaxim, were more frequently used to treat CAP in inpatients in our study (291, 79.7%); this was also the case in Syria (Damascus) (Abdullah Almouslli et al., 2023). However, in Saudi Arabi (Sultan Al Albuhairi et al., 2020) Amoxicillin Clavulanate was administered to most patients (57.9%), with Ceftriaxone closely after (30%), and in the north of England (Julia E. Clark, 2006), second-generation Cephalosporins, such as cefuroxime, were the most frequently used intravenous antibiotics in 61% of cases. The usage of antibiotics depends on local guidelines and local bacteria resistance.

About a quarter of our patients 84 (23%) were admitted to an intensive care unit and were mainly infants 61 (72.6%). These findings were also reported in Tunis (Samia Hamouda et al 2016).

The median hospital stay was 3.5 days, corresponding to findings from Beirut, Lebanon (Rim Tan-nous et al 2020).

CONCLUSION

We conclude that infants were the predominant age group that developed CAP and required PICU admission, with a higher incidence throughout the winter months.

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Author contributions: Contribution is equal between authors.

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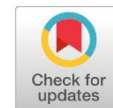
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Research Article

⁶Open Access



Perioperative Use of Intravenous Lidocaine Infusion to Decrease Postoperative Opioids in Colorectal Surgery: A Randomized Prospective Study

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Abstract

Pain is defined as an unpleasant sensory and emotional sensation provoked by real tissue damage and manifested by autonomic, psychological, and behavioral reactions. Improvement of postoperative pain control remains a significant challenge among clinicians. 40 patients aged 30-60 years, ASA 1-2 scheduled for colorectal surgery, were divided into two groups 20 patients each. Lidocaine group: (n= 20) received bolus intravenous lidocaine 20 min before incision with a dose of 1.5mg/kg followed by lidocaine infusion with a dose of 1.5mg/kg/h. Control group: (n= 20) receive intravenous lidocaine only. After premedication with a bolus dose of lidocaine at induction, the heart rate was lower in the interventional group compared with the control one until 12 hours post-operatively, then returned to be equal by 24 hours. Between recovery and one hour postoperative, intraoperative serial differences were significant only for the intervention group. After premedication and during the operation until 24 hours, postoperative mean blood pressure was significantly higher among controls. This returns to be equal by 48 hours and beyond. The postoperative VAS score and analgesic requirements were significantly lower in the lidocaine infusion group. Perioperative lidocaine infusion provides analgesia, low pain score, and decreases postoperative opioid consumption in laparoscopic colorectal surgery.

Keywords: Anesthesia, Lidocaine infusion, Colorectal surgery, Pain, Analgesia.

INTRODUCTION

Pain is a complex of unpleasant sensory, emotional, and cognitive sensations caused by real tissue damage (Terman GW, et al. 2001). It is provoked by a noxious stimulus that gives impulses that reach the brain through the ascending pathway in the spinal cord. The primary afferents called the nociceptors are located in the nerve endings and end in the dorsal horn in the spinal cord. These nerves could be classified into small myelinated A-delta fibers and unmyelinated C fibers. The nociceptors when stimulated produce action potential that is transferred through these primary afferents, leading to the release of excitatory amino acids, neurotrophins, and peptides such as substance P, neurokinin A, and calcitonin gene-related peptide (CGRP) from the nerve endings in the dorsal



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horn of the spinal cord (Vranken JH 2012). The communication between the neurons of the pain pathways is mainly via chemical neurotransmitters. Several neurotransmitters and their receptors transmit and modulate the sensation of pain. Painful damage causes inflammatory changes that lead to the activation of inflammatory mediators that cause depolarization of the nociceptive membrane by the opening up of voltage and ligand-gated ion channels (Aggugia M. 2003).

The N-Methyl-D- aspartate (NMDA) receptors have a great role in the propagation of chronic pain and it is responsible for hyperalgesia and allodynia sensations (Woolf CJ. 2011) (Coull JA, et al. 2005). The gamma-aminobutyric acid (GABA) secreted by the inhibitory neurons, affects pain transmission at the superficial layers of the dorsal horn by presynaptic inhibition of pain fibers and blocks the release of excitatory amino acids (Gwak YS, et al. 2011)

Two mechanisms modulate the feeling of pain within the central nervous system, which are the inhibitory and excitatory mechanisms. The majority of them are inhibitory and are activated with the initiation of nociceptive information to decrease pain sensations (Gassner M, et al. 2009).

The descending pathway exists from the nucleus raphe magnus has inhibitory effects via activating 5-HT_{1A} and 5-HT₇ receptors and excitatory effects by 5-HT_{2A} and 5-HT₃ receptors) on pain transmission (Doly S, et al. 2005). Trauma caused by surgery results in the release of cytokines initiating local inflammatory responses and promoting tissue healing (Lin E, et al. 2000).

The degree of tissue damage is correlated with the increase of Interleukin-6 (IL-6), which is detected early as an initial response to injury (Gebhard F, et al. 2000). Lidocaine is an amide type of local anesthetic that has an antiarrhythmic, analgesic, anti-inflammatory, and anti-hyperalgesia effect. It blocks intracellular sodium channels of neurons, interrupting the propagation of impulses in neural axons, and inhibits NMDA activation by blocking glutamate/glycine, and by inhibiting protein kinase C (Hahnenkamp K, et al. 2006).

Other studies have reported that IV lidocaine can cause the reduction of cytokines, and postoperative pain intensity (Kuo CP, et al. 2006). Furthermore, low doses of intravenous lidocaine (plasma level below 5µg/ml) are ineffective on normal nerve conduction and are associated with fewer opioid side effects (Wu CT, et al. 2005). The sodium channels are the main site of action of lidocaine (Canavero S, et al. 2006). The painkiller effect and anti-inflammatory action can act via calcium and potassium channels and receptors through G protein coupling (Heavner JE 2007). Some lidocaine metabolites, like monoethylglycinexylidide (MEGX), may have an analgesic effect (Werdehausen R, et al. 2012).

Surgical procedures on the abdomen have a higher incidence of postoperative pain and gastrointestinal motility dysfunction. Laparoscopic colorectal surgery has become a common surgery, as it is associated with less pain and less analgesic use, low incidence of infection, rapid recovery, and short hospital stay (Lloyd GM, et al. 2010). Proper pain control is the mainstay of postoperative care that facilitates early mobility and feeding (White PF 2002). Other studies used preoperative intravenous lidocaine infusion as an alternative approach and have reported a beneficial effect on pain management postoperatively and significantly improved the general outcomes including the spare consumption of opioids (Lauwivk S, et al. 2008), and early recovery of bowel mobility (Harvey KP, et al. 2009), particularly after urological surgeries (Groudine SB, et al. 1998), and shortens the hospital stay after colorectal surgeries (Herroedr S, et al. 2007).

Intravenous lidocaine infusion is used as an adjunct to provide anesthesia with less opioid consumption, inhalation, and neuromuscular-blocking agents (Dennis PB, et al. 2020).

The vision of this study is to compare with other studies and research results, considering the differences in environmental factors, resources, size of samples, dose of lidocaine, and duration of surgery. The primary endpoint of this study was to evaluate postoperative pain scores and the need for postoperative analgesia.

MATERIALS AND METHODS

After obtaining our institutional ethics committee approval and written informed consent from each patient, 40 male patients aged 30-60 years, ASA 1-2 scheduled for colorectal surgery were involved in this randomized prospective study divided into two groups, 20 patients each.

The participants included in this study had no hepatic, renal, or cardiac diseases or allergies to local anesthetics.

Patients with intraoperative hypotension (mean blood pressure <60mmHg) or bradycardia (heart rate < 40 beats/min), urticaria, or arrhythmia associated with lidocaine infusion were excluded.

Both groups were premedicated by midazolam to overcome any effect of anxiety on vital signs.

Lidocaine group: (n= 20) received bolus IV lidocaine 20 min before incision with a dose of 1.5mg/kg followed by lidocaine infusion of 1.5mg/kg/h until skin closure.

Control group: (n= 20) were untreated with lidocaine.

General anesthesia was induced with propofol 2mg/kg IV, rocuronium 0.8mg/kg IV with oxygen, and sevoflurane mask ventilation followed with oral endotracheal intubation.

Anesthesia was maintained with sevoflurane with oxygen and medical air 1L: 1L.

Fentanyl was given to the patients in either group during the maintenance of anesthesia as needed according to vital signs. Patients were monitored throughout the operation with BP, HR, SPO₂, end-tidal sevoflurane, and end-tidal CO₂. Sevoflurane concentration was adjusted according to the hemodynamic values. HR and BP were maintained within 20% of preoperative values. End-tidal CO₂ was between 35-45 mmHg. Perioperative fluid with lactate ringer solution at a rate of 6-8 ml/kg/h. Intraoperatively, the vital signs are taken and recorded every 5 minutes in the first 30 minutes then every 15 for the rest of surgery. At the end of the surgery, the muscle relaxant was reversed with sugammadex (2mg/kg). In the post-anesthesia care unit (PACU) postoperative pain control with IV tramadol was provided within 20 min after surgery and supplemented after recovery as needed. The total amount and frequency of analgesics and opioid-associated side effects such as nausea and vomiting were registered. Postoperative pain was assisted by a visual analog scale (VAS) which ranged from 0-10 at 1st, 2nd, 3rd, 4th, 5th, 6th, 12th, 24th, 48th, and 72nd hours post-operatively. For statistical analysis, SPSS version 20.0 was used. The parametric variables are presented as mean $\pm$ SD or frequency (%) and analyzed by student t-test. Statistical analysis is performed with an ANOVA test. P< 0.05 was considered as statistically significant. This study aims to evaluate the effects of perioperative intravenous lidocaine infusion on postoperative pain and opioid consumption in patients undergoing colorectal surgeries.

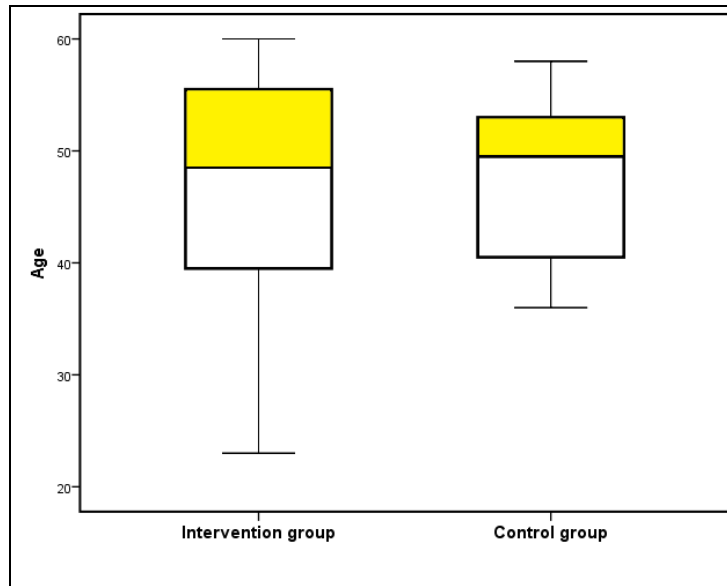
RESULTS

Both groups were matched regarding age. Age was homogeneous across study groups, Table (1) and Figure (1). No patient was excluded from the study, as all fit the inclusion criteria.

Table (1). Age parameters of study groups

Parameter	Group	
	Intervention group	Control group
Mean	46.85	47.60
SD	10.241	7.185

t = -0.268, P = 0.790 (Non-significant)

**Figure (1).** Plot of age parameter across study groups

When comparing the heart rate among both groups, there are no differences between the two groups in baseline heart rate before premedication. After premedication with a bolus dose of lidocaine and induction, the heart rate was lower among the interventional group compared with the control one until 12 hours postoperative. This returns to be equal by 24 hours and beyond. The intraoperative serial difference was significant along perioperative measurements for both groups (Friedman test $X^2 = 27.76$, $P < 0.001$ for controls versus Friedman test $X^2 = 88.742$, $P < 0.001$ for intervention group), Table (2). Between recovery and one-hour post-operative, Intraoperative serial difference was significant only for the intervention group (Wilcoxon signed rank test

$Z = -1.132$, $P = 0.258$ for controls versus $Z = -2.953$, $P = 0.003$ for the intervention group). Figure (2).

Table (2). Serial preoperative and intraoperative heart rate measurement inter-group comparison

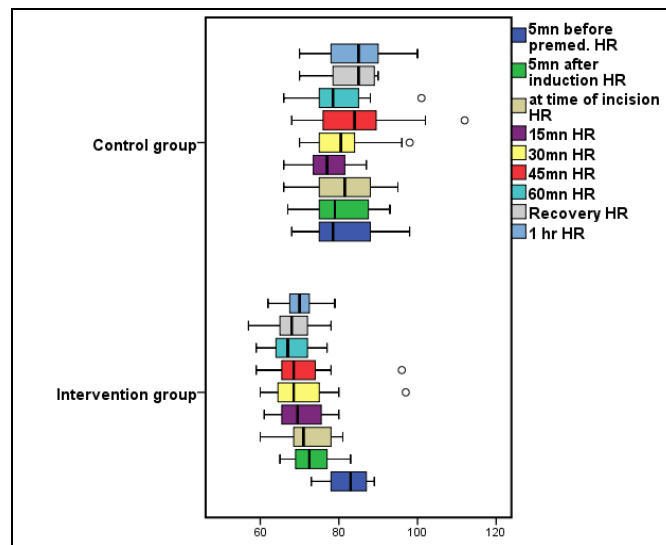
Time	Mean (SD)		T	P
	Intervention group	Control group		
5mn before premed.	82.15 (5.214)	80.75 (9.066)	0.599	0.554
5mn after induction	72.80 (5.248)	80.50 (7.508)	-3.759	0.001*
at the time of incision	72.30 (5.686)	81.45 (8.042)	-4.155	<0.001*
15mn	70.30 (5.555)	77.35 (5.631)	-3.986	<0.001*
30mn	70.45 (8.256)	81.20 (7.784)	-4.237	<0.001*
45mn	69.80 (7.851)	85.30 (10.931)	-5.151	<0.001*
60mn	67.70 (5.172)	80.20 (7.509)	-6.131	<0.001*
Recovery	67.80 (5.317)	83.25 (6.180)	-8.475	<0.001*

* The difference is significant at the level of confidence 95% or higher.

Table (3). Serial post-operative heart rate measurement inter-group comparison

Time	Mean (SD)		T	P
	Intervention group	Control group		
1	70.25(4.387)	84.35(8.381)	-6.666	<0.001*
4	73.90(4.621)	80.05(6.452)	-3.465	0.001*
5	74.80(4.444)	81.55(6.493)	-3.837	<0.001*
6	76.15(4.727)	82.45(6.962)	-3.348	0.002*
12	77.30(4.635)	82.70(6.775)	-2.942	0.006*
24	78.60(4.173)	81.35(6.011)	-1.681	0.101
48	79.85(4.499)	80.20(6.330)	-0.202	0.841
72	80.75(4.494)	80.05(6.403)	0.400	0.691

* The difference is significant at the level of confidence 95% or higher.

**Figure (2).** Plot for heart rate serial measurements in both study groups

There is no difference in baseline mean blood pressure between the two groups, but after premedication, induction, and during the operation until 24 hours, postoperative mean blood pressure was significantly higher among the control group. This returns to be equal by 48 hours and beyond. Serial differences were significant along intraoperative measurements for both groups (Friedman test $X^2 = 77.53$, $P < 0.001$ for controls versus Friedman test $X^2 = 91.2$, $P < 0.001$ for the intervention group). Table (4). Between recovery and one-hour post-operative, serial differences were significant only for the intervention group (Wilcoxon signed rank test $Z = -1.072$, $P = 0.284$ for controls versus $Z = -3.488$, $P < 0.001$ for the intervention group), Figure (3).

Table (4). Serial preoperative and intraoperative mean blood pressure measurement groups comparison

Time	Mean (SD)		T	P
	Intervention group	Control group		
5min before premedication	98.151(1.189)	102.10 (6.640)	-1.358	0.183
5 min after induction	86.05 (5.605)	91.45 (5.735)	-3.011	0.005*
time of incision	85.959(5.671)	93.90 (5.857)	-4.361	<0.001*
15 min	83.85(6.141)	92.70 (4.589)	-5.162	<0.001*
30 min	83.30(8.986)	97.90 (7.490)	-5.582	<0.001*
45 min	82.45(6.653)	98.80 (6.396)	-7.923	<0.001*
60 min	79.45(5.615)	96.05 (4.893)	-9.968	<0.001*
Recovery time	79.75(5.893)	99.35 (5.489)	-10.88	<0.001*

* The difference is significant at a level of confidence of 95% or higher.

Postoperative mean blood pressure was tremendously lower among the interventional group until 24 hours and then there were no differences.

Table (5). Serial post-operative mean blood pressure measurement inter-group comparison

Time (hour)	Mean (SD)		T	P
	Intervention group	Control group		
1	84.95 (5.951)	98.40 (6.116)	-7.048	<0.001*
4	89.25 (6.812)	97.55 (6.219)	-4.024	<0.001*
5	90.65 (5.480)	98.70 (6.053)	-4.409	<0.001*
6	91.15 (6.150)	99.30 (6.530)	-4.063	<0.001*
12	93.25 (6.463)	99.60 (5.276)	-3.404	0.002*
24	94.95 (6.403)	99.90 (5.515)	-2.620	0.013*
48	96.10 (6.874)	98.65 (6.310)	-1.222	0.229
72	97.10 (6.782)	98.30 (6.097)	-0.588	0.560

* The difference is significant at a level of confidence of 95% or higher.

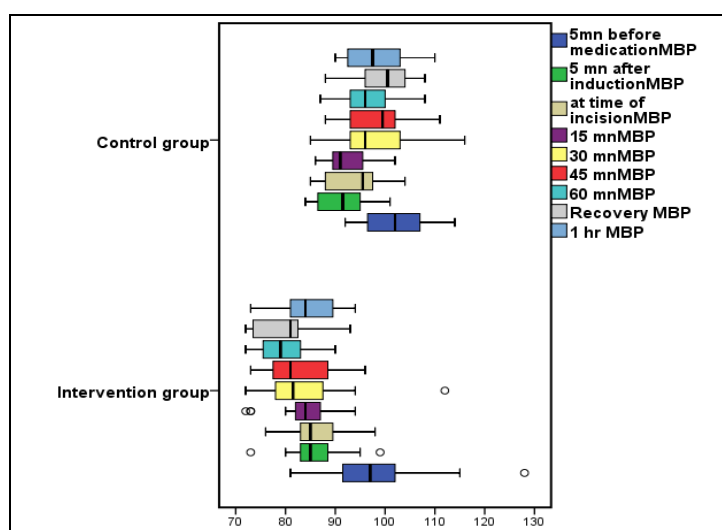


Figure (3). Plot for mean blood pressure serial measurements in both study groups

The postoperative VAS was significantly lower in the lidocaine group Table (6), and also decreased the analgesic requirements in the lidocaine group as compared with the control group postoperatively Table (8), and also, noted that rocuronium was used less frequently in the interventional group Figure (9).

Table (6): VAS parameters of study groups

Parameter	Group	
	Intervention group	Control group
Mean	1.47	3.19
SD	0.46	0.22

t = -15.081, P <0.001 (Significant)

The average of the visual analogue scale was lower among the interventional group.

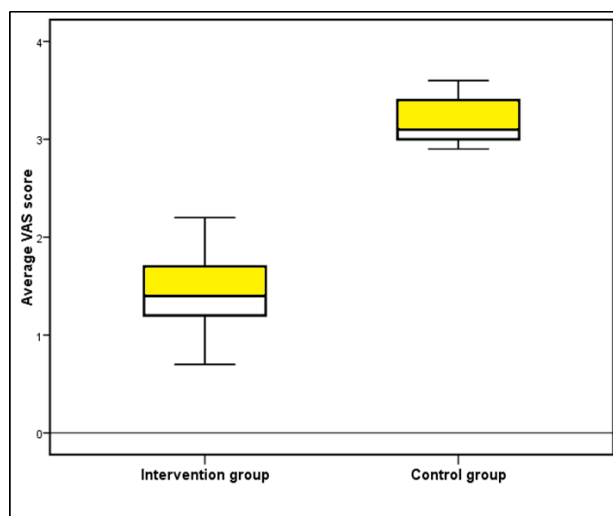


Figure (4). Plot of average VAS score parameters across study groups.

The 72 hours postoperative VAS was significantly higher among control except for hour 3. Table (7). The intragroup serial difference was significant only for the control group (Friedman test $X^2 = 12.686$, $P = 0.002$ for controls versus Friedman test $X^2 = 4.0$, $P = 0.135$ for the intervention group), Figure (5).

Table (7). Serial postoperative visual analogue scale measurement inter-group comparison

Time (hour)	Mean (SD)		T	P
	Intervention group	Control group		
1	0.10 (0.308)	3.70 (1.895)	-8.388	<0.001*
2	0.00 (0.000)	2.05 (2.585)	-3.547	0.002*
3	0.00 (0.000)	0.50 (1.539)	-1.453	0.163
4	0.5 (5.686)	2.4 (0.883)	-7.400	<0.001*
5	1.00 (1.124)	3.50 (1.395)	-6.240	<0.001*
6	1.05 (1.099)	3.55 (1.276)	-6.638	<0.001*
12	2.5 (5.999)	4.4 (0.883)	-6.208	<0.001*
24	3.00 (1.298)	4.2 (0.410)	-3.943	0.001*
48	3.2 (0.834)	3.7 (5.444)	-2.604	0.014*
72	3.2 (5.786)	3.9 (0.308)	-3.442	0.002*

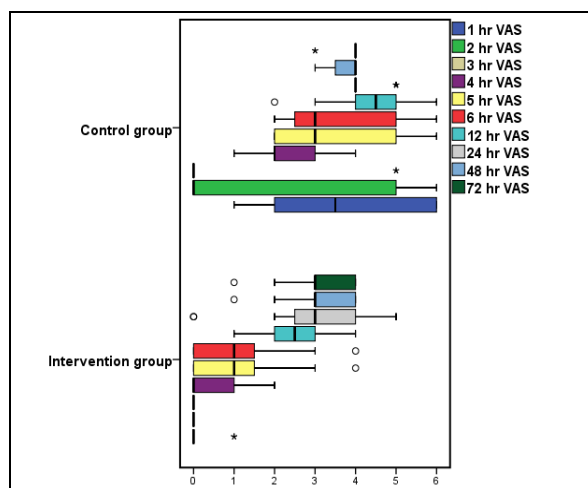


Figure (5). Plot for visual analogue scale serial measurements in both study groups.

The mean of required tramadol doses in the control group was almost more than half that of the interventional group.

Table (8). Total tramadol dose parameters of study groups

Parameter	Group	
	Intervention group	Control group
Mean in mg	662.50	1152.50
SD in mg	129.650	105.724

$t = -13.099$, $P < 0.001$ (Significant)

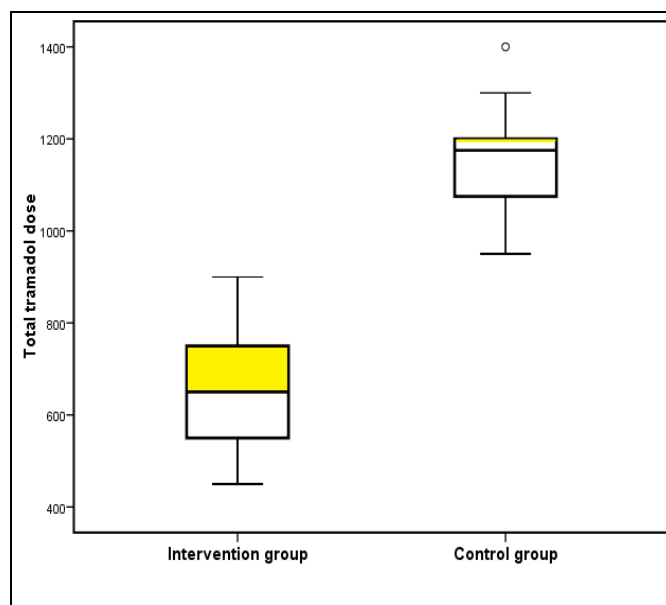


Figure (6). Plot of total required tramadol parameters across study groups

During 10 hours postoperative, the dose of tramadol was significantly higher among control except for hours 3, 4, and 8, Table (9). The intragroup serial difference was significant only for control group (Friedman test $X^2 = 13.6$, $P = 0.004$ for controls versus Friedman test $X^2 = 3.0$, $P = 0.392$ for the intervention group), Figure (7).

Table (9). Serial total doses of tramadol inter-group comparison

Time (hour)	Mean (SD)		T	P
	Intervention group	Control group		
1	0.00 (0.000)	42.50 (46.665)	-4.073	0.001*
2	0.00 (0.000)	35.00 (46.169)	-3.390	0.003*
3	0.00 (0.000)	7.50 (24.468)	-1.371	0.186
4	2.501 (1.180)	0.00 (0.000)	1.000	0.330
5	2.501 (1.180)	30.00 (41.039)	-2.891	0.009*
6	5.001 (5.390)	37.50 (48.327)	-2.866	0.009*
7	67.50 (33.541)	95.00 (35.909)	-2.503	0.017*
8	112.50 (58.208)	140.00(50.262)	-1.599	0.118
9	222.50 (47.226)	385.00 (36.635)	-12.159	<0.001*
10	250.00 (51.299)	380.00 (41.039)	-8.850	<0.001*

* The difference is significant at the level of confidence 95% or higher.

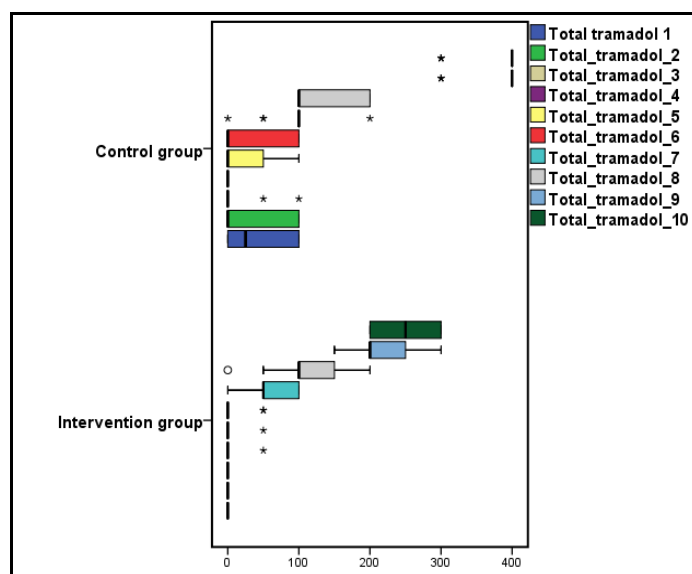


Figure (7). Plot for tramadol dose serial measurements in both study groups

The control group has a higher frequency of rocuronium usage. Intervention group; 1 – 5 times per patient, mean = 2.4 (SD=1.1) and median of 2 times per patient. Control group; 3 – 6 times per patient, mean = 4.4 (SD= 0.9) and median of 4.5 times per patient.

The difference was statistically significant (Mann-Whitney U test statistic = 38.5, $P < 0.001$) Figure (8). Highest proportions of patients in the intervention group were reported with the least frequency of rocuronium use and the inverse in the control group, Figure (9).

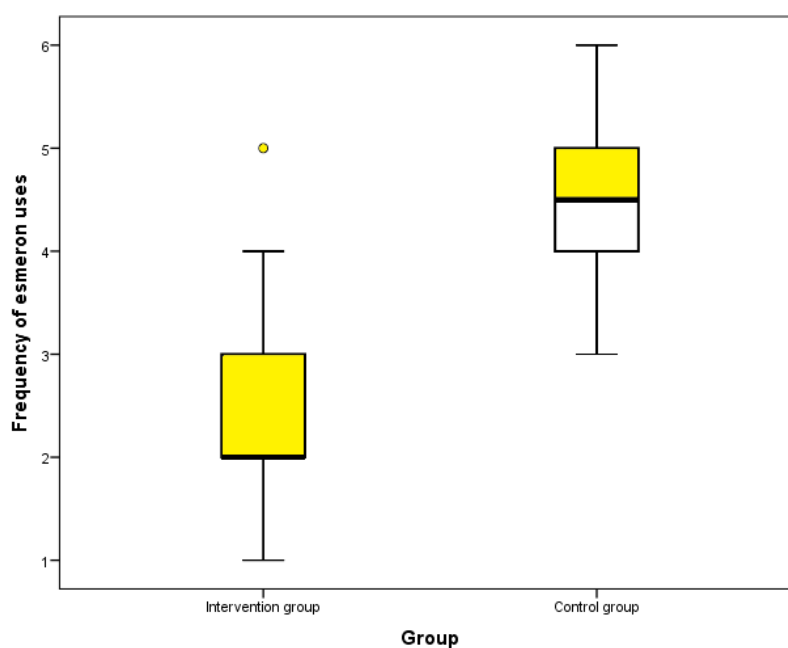


Figure (8): Plot for frequency of rocuronium use in both study groups.

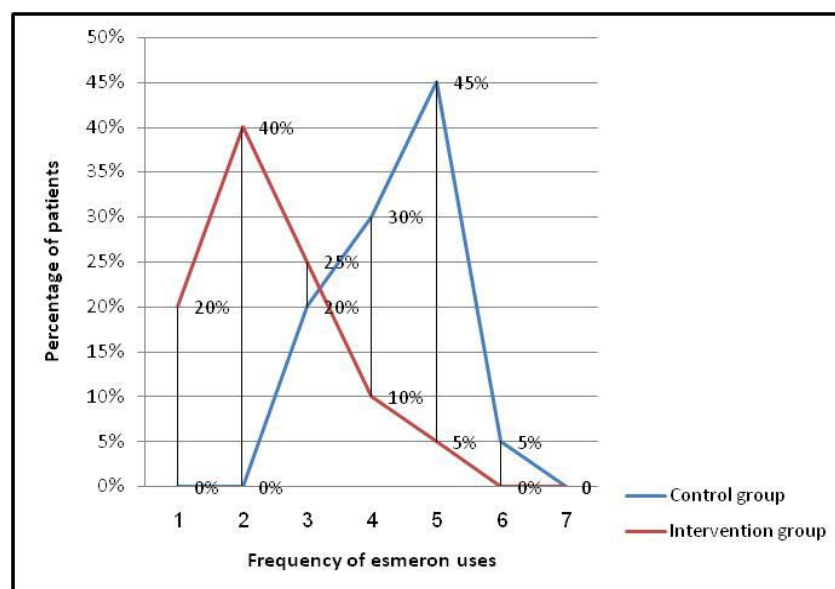


Figure (9). Plot for rates of patients in both study groups according to each frequency of rocuronium usage.

DISCUSSION

The current study suggests the use of perioperative lidocaine infusion in patients undergoing laparoscopic colorectal surgeries, and that laparoscopic surgery improves postoperative analgesia and reduces postoperative opioid consumption. The uses of lidocaine beyond local and regional tissue anesthesia are well established. Given intravenously, it is effective in obtunding the sympathetic response to laryngoscopy and reducing the pain of propofol injection. (Keats AS, et al. 1951) first documented a positive analgesic effect on postoperative pain. Investigation and interest in perioperative IV local anesthetic infusion has continued. A systematic review of multiple studies done in 2010 documented a low incidence of pain when IV lidocaine infusions were given during general anesthesia (McCarthy GC, et al. 2010). According to this study, IV lidocaine infusion in the perioperative period is safe and results in a low incidence of pain, reduced postoperative analgesic consumption, and decreased intraoperative anesthetic requirement.

The effect of lidocaine might be due to the suppression of neuronal excitability in dorsal horn neurons, inhibiting the spike activity, amplitude, and conduction time in both myelinated A and unmyelinated C fibers. The dosage of lidocaine in this study was similar to a study by (Groudine, et al. 1998). The current study revealed a significantly low incidence of tachycardia and MBP in the interventional group when compared with the control group. This finding is in accordance with (Lauwivk S, et al. 2008). Whereas (Kaba A, et al. 2007) and (Groudine SB, et al. 1998), didn't find any significant analgesic effect of lidocaine infusion.

CONCLUSION

Perioperative lidocaine infusion has a beneficial effect on patients who have undergone laparoscopic colorectal surgery, provides analgesia, low pain score, and decreases postoperative opioid consumption.

Based on the results of this study, it is recommended to consider intravenous lidocaine perioperatively to provide analgesia, low pain score, and decrease postoperative opioid consumption in laparoscopic colorectal surgery.

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Author contributions: Contribution is equal between authors.

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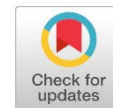
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Research Article

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The Types of Congenital Heart Disease in Down Syndrome Patients: Single-center Review of Cases in Benghazi, Libya

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Abstract:

Congenital heart disease (CHD) is a primary cause of mortality among children with Down syndrome (DS). CHD prevalence and types in DS vary worldwide, likely influenced by socio-demographics, genetics, and geography. This study evaluates CHD occurrence and types among children with DS in eastern Libya from 2010 to 2017. Of 181 children with DS examined via echocardiogram, 67 (37%) had normal cardiac anatomy, while 114 (63%) had CHD. Among the CHD cases, 88 (77%) had single cardiac anomalies, and 26 (22.8%) had multiple defects. The most common single defect was atrial septal defect (ASD), present in 39/114 (34%), followed by an atrioventricular septal defect (AVSD) in 23/114 (20%) and ventricular septal defect (VSD) in 11/114 (6.9%). Patent ductus arteriosus (PDA) was identified in 5 cases (4%), tetralogy of Fallot (TOF) in 4 cases (3.5%), mitral regurgitation (MR) in 1.7%, aortic regurgitation (AR) in 0.9%, Ebstein's anomaly in 0.9%, and double outlet right ventricle (DORV) in one case (0.9%). This study supports that CHD distribution in DS varies by ethnicity and region, with ASD being the most common. No association with maternal age was found. Paternal consanguinity in tribal societies may contribute to chromosomal abnormalities and CHD.

Keywords: Down Syndrome, Congenital Heart Disease, Ventricular Septal Defect, Patent Ductus Arterioles, Atrial Septum Defect.

INTRODUCTION

Down syndrome, or trisomy 21, is the foremost prevalent chromosomal anomaly, occurring at an evaluated rate of 16 per 10,000 live births (Weijerman et al., 2010). There is a well-established association between Down syndrome and congenital cardiac defects; nearly 50% of children with Down syndrome have congenital heart disease, which increases the risk of mortality and morbidity, particularly within their first year (Dimopoulos et al., 2023; Weijerman et al., 2010). The estimated number of children in Libya with moderate to severe congenital heart disease (CHD) who require surgical or medical intervention within their first year of life is around 500 (Aburawi, 2006). A study on CHD frequency in children with Down syndrome in western Libya indicated that atrial septal defect (ASD) is the foremost common CHD in DS (Elmagrpy et al., 2011).



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Reports suggest that the frequency of congenital heart disease (CHD) in children with Down syndrome may vary geographically. In Western literature, as well as in Turkey and Morocco, atrioventricular septal defect (AVSD) is the most common CHD (Benhaourech et al., 2016; Dimopoulos et al., 2023; Nisli et al., 2008; Tandon & Edwards, 1973). Conversely, studies from other Arab countries show different prevalence patterns. For instance, in Egypt, ventricular septal defect (VSD) is the most common CHD in patients with trisomy 21. In studies from western Saudi Arabia and Ethiopia, unique patterns emerge, such as patent ductus arteriosus (PDA) being the most frequent single defect. Research from Sudan and Nigeria reveals CHD patterns similar to those in developed nations, with AVSD being the most common CHD among children with Down syndrome (Ali, 2009; Wahab et al., 2006). In developing countries, the diagnosis of Down syndrome typically relies on phenotypic features. Recently, maternal age has not been considered a primary risk factor for Down syndrome; other factors, such as maternal smoking and obesity, are now implicated (Animasahun et al., 2016; Ferguson - Smith & Yates, 1984).

MATERIALS AND METHODS

Settings:

The study was retrospective and descriptive. We reviewed patient medical files from June 2010 to July 2017. The genetic clinic registry documented 222 cases of Down syndrome within seven years. All these patients' charts included physical examinations, echocardiography, abdominal and brain ultrasound, blood tests for thyroid function, and celiac screening. During the echocardiography screening, we utilized the VIVID 5 echocardiographic assessment.

Data Collection:

The study was performed at the Genetic Clinic of Hawari General Hospital in Benghazi, a tertiary and university hospital. We reviewed seven-year patient records from June 2010 to June 2017, including all Down syndrome (DS) cases. Data Collection Procedure: data were manually extracted from the clinic logbooks and patient records and transferred to a structured questionnaire. Collected data included the patient's current age, sex, parental contact information, age at initial diagnosis, history of consanguinity, maternal age at conception, and echo report details. The diagnosis was established based on phenotypic clinical features, which include characteristics such as mongoloid faces, single palmar crease, protruding tongue, a depressed nasal bridge, flat occiput, small and low-set ears, upward-slanted palpable fissure in eyes, epicanthic fold, hypotonia. Short neck and Chromosomal studies were also considered in some cases to confirm the diagnosis.

Statistical Analysis:

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 23

RESULTS

Within the seven-year study period, the genetic clinic saw 312 patients. Of those, 222 had Down syndrome (71.2%), and of those, only (181/222) had an echocardiography examination. The patients' geographical distribution was as follows: 73% from Benghazi, 14% from other cities in the eastern part of Libya, 8% from the south of Libya, and 4% from the west of Libya, illustrated in Figure 1.

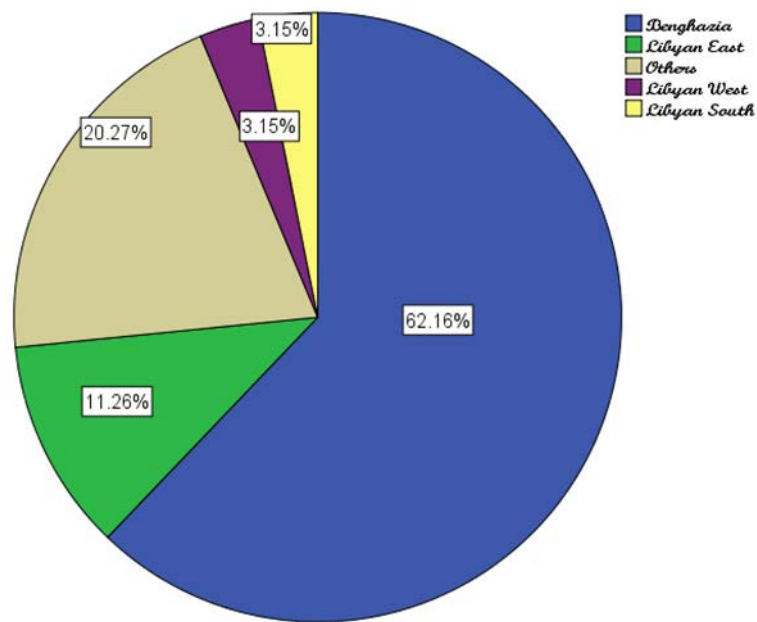


Figure (1). The geographical distribution of the patient

The presenting age at the clinic was 57% neonates, 22% less than one year, and 10% between one and five years. Seven % were between 5 and 10 years old. Lastly, 3% were over 10 years old, as shown in Figure (2).

There were 118 males and 104 females; the male-to-female ratio was 1.1:1.

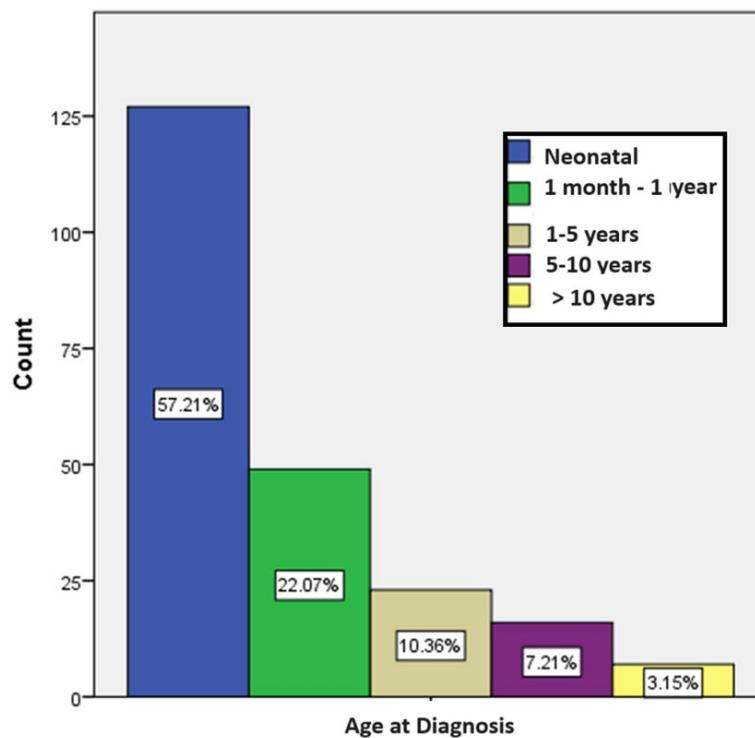


Figure (2). The age of diagnosis of congenital heart disease.

The chromosomal study was done in 42/222 36 patients (86%) were Trisomy 21: (47XX or 47XY), four patients were translocation (two have 14, 21 translocations, one has 13, 21 translocations, and one has translocation of 18, 21), and two patients were mosaic type.

The mothers' ages were recorded in 195 patient files. 50/195 (25.5%) of mothers were more than 35, and 145/195 (74%) were less than 35 when they had their baby with Down syndrome. A family history of consanguinity was positive in 83% of patients with DS, and 16% had no history of consanguinity.

Echocardiography examination results, illustrated in Figure (3), were conducted on 181 out of 222 patients, revealing that 114 out of these 181 patients (63%) had congenital heart disease (CHD), and 67 out of 181 (37%) exhibited normal cardiac anatomy. Of those diagnosed with CHD, 88 individuals (77%) had a single cardiac defect, while the remaining 26 cases (23%) had multiple lesions. The most frequently occurring single lesion was atrial septal defect (ASD), which was observed in 39 patients (34%), followed by atrioventricular septal defects (AVSD) in 23 patients (20%) and ventricular septal defect (VSD) in 11 patients (9.6%).

Less commonly, patent ductus arteriosus (PDA) was identified in six cases (5%), while tetralogy of Fallot (TOF) was present in four cases (3.5%). Mitral regurgitation (MR) was found in two cases (1.8%), aortic regurgitation (AR) in one patient (0.9%), and Ebstein's anomaly in 0.9% of cases. In addition, DORV TGA one patient with 0.9% ASD was frequently found in association firstly with PDA in 13 cases (11%), followed by association with VSD in 7 cases (6%). One patient presented with both ASD and pulmonary stenosis (0.9%). VSD was found in 11/114 patients (9.6%) as single lesion VSD was found to be coexistent with ASD in 7 cases (6%) and with PDA in 5 cases (4.4%). Upon reviewing the medical files, we found that only 9 patients had surgical intervention 4%, 3 patients had transcatheter intervention 1.4%, and one patient died.

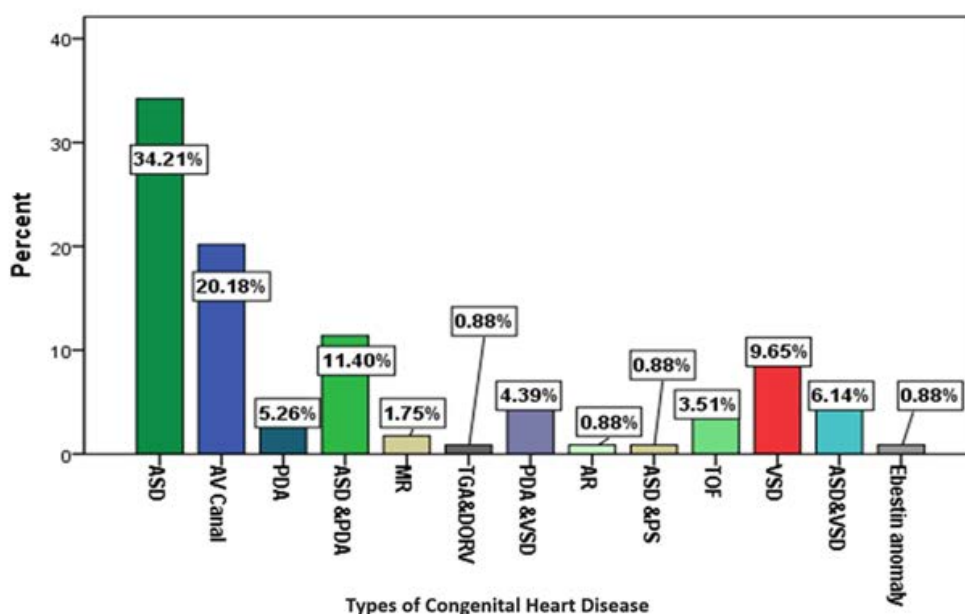


Figure (3). The frequency distribution of the various types of congenital heart disease.

DISCUSSION

The predominance of congenital heart disease (CHD) in children with trisomy 21 at our genetic clinic is remarkably high, at 62%. This figure is considerably higher than the 45% reported in Tripoli, in the western part of Libya (Elmagrpy et al., 2011). Furthermore, the prevalence observed in our study exceeds the 36.9%, 50%, and 51.7% reported in Egypt, Brazil, and Qatar, respectively (Bermudez et al., 2015; El-Gilany et al., 2017; Wahab et al., 2006). However, it is lower than the prevalence rates reported in western Saudi Arabia (86.6%) and Nigeria (95.8%) (Al-Aama et al., 2012; Susan & Chiemerie, 2022).

The high prevalence of congenital heart disease (CHD) in our study can be attributed to several factors. The most significant is early diagnosis, with over 57% of our sample diagnosed during the neonatal period, which included cases of small atrial septal defect (ASD) and patent ductus arteriosus (PDA). Additionally, 83% of DS patients in our study had a history of consanguinity, while 16% had no consanguinity (El-Gilany et al., 2017; Elmagrpy et al., 2011; Sharifi et al., 2018). Another factor is that the paperwork of our genetic clinic was mandated by the government to obtain financial aid for these populations. This resulted in a high early referral rate and early cardiac screening.

Early diagnosis in our study relied on the characteristic physical features of children with trisomy 21, which presents a study limitation. Although genetic testing was unavailable in our hospital, 42 out of 222 patients (19%) obtained chromosomal studies through private facilities. Of these, 36 patients (86%) had trisomy 47XX or 47XY, 4 had a translocation, and 2 exhibited a mosaic pattern, consistent with a study in Qatar showing 98% of participants have regular trisomy (Wahab et al., 2006).

Among the cardiac anomalies observed in children with trisomy 21 in our study, isolated cardiac defects were found in 76.8% of cases, compared with 65%, 70.4%, 29%, 23%, and 80.4% reported in Tripoli, Morocco, Egypt, Saudi Arabia, and Guatemala, respectively (Al-Aama et al., 2012; Benhaourech et al., 2016; El-Gilany et al., 2017; Elmagrpy et al., 2011; Vida et al., 2005). Atrial septal defect (ASD) is the most common congenital heart disease (CHD) in our study, similar to findings in western Libya, Korea, and Brazil (Bermudez et al., 2015; Elmagrpy et al., 2011; Kim et al., 2014). ASD, whether isolated or combined with other defects, accounted for 51.8% of cases. Atrioventricular septal defect (AVSD) was the second most common CHD in our study at 20%, while in European countries, the USA, Turkey, Morocco, and Sudan, AVSD is the most prevalent CHD (Ali, 2009; Benhaourech et al., 2016; Dimopoulos et al., 2023; Nisli et al., 2008; Weijerman et al., 2010). In contrast, other countries, such as Egypt and Afghanistan, report ventricular septal defect (VSD) as the most common CHD (El-Gilany et al., 2017; Sharifi et al., 2018). The isolated VSD rate in our study, however, was only 9.6%.

In other regions, such as western Saudi Arabia, Ethiopia, and Guatemala, patent ductus arteriosus (PDA) is the most common congenital heart disease (CHD) (Al-Aama et al., 2012; Muntha & Moges, 2019; Vida et al., 2005). In our study, isolated PDA accounted for only 5% of cases, while a combination of ventricular septal defect (VSD) and PDA occurred in 4.1% of cases. The most common isolated cyanotic CHD was Tetralogy of Fallot (TOF), representing 3.5% of cases, which is comparable to rates reported in Sudan (5%), Nigeria (8.3%), and Ethiopia (2.6%) (Ali, 2009; Muntha & Moges, 2019; Susan & Chiemerie, 2022).

Our study reveals a higher prevalence of trisomy 21 among children born to younger mothers. Maternal age was documented in 195 patient files, with 145 mothers (74%) under 35 years old at the time of their child's birth with Down syndrome, while 50 mothers (25.5%) were over 35. This con-

trasts with European studies suggesting that advanced maternal age increases the risk of chromosomal aberrations, especially autosomal trisomies (Ferguson - Smith & Yates, 1984). However, reports from Egypt (El-Gilany et al., 2017), Nigeria (Animasahun et al., 2016), and a recent systematic review and meta-analysis have identified a significant correlation between CHD and other risk factors, such as maternal obesity, active and passive smoking, diabetes, and exposure to organic solvents during pregnancy (Wu et al., 2023).

CONCLUSION

Our study confirms that the distribution of CHDs in children with trisomy 21 may vary based on ethnicity and geographical regions. We found a significantly elevated occurrence of CHDs in children with trisomy 21 in comparison to national and international levels; ASD was the most common lesion. There was no clear association between maternal age and DS; another factor that may be contributing is that paternal consanguinity may play a significant role in the development of chromosomal aberration and CHD in tribal societies. We need further research to explore other maternal factors that may influence the incidence of DS and CHD in young mothers.

ETHICS

This study is non-interventional and poses no risk to patients and families.

Duality of interest: The authors declare that they have no duality of interest associated with this manuscript.

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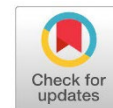
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Research Article

⁶Open Access



Study of Risk Factors for *Entamoeba Histolytica* in Preschool Children: A Questionnaire Survey

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Abstract

Amebiasis is a parasitic infection of the intestines caused by a protozoa *Entamoeba histolytica* (*E. histolytica*) that mainly leads to diarrhea. A study was conducted to determine the prevalence of risk factors for *Entamoeba histolytica* infection. A study was carried out to assess the occurrence of risk factors for *Entamoeba histolytica* infection among children in the western region of Libya. A total of 55 children, 27 male and 28 female, with an average age of 2 and 5 years, were included in this study. Their mothers were interviewed using a structured questionnaire survey. The majority (61.82%) consumed water that originated from treated water, and most, (81.82%) consumed washed fruits before eating. All respondents consumed Well-cooked meat, washed their hands before eating (70.91%), while in contact with soil (87.27%), washed their hands after entering the bathroom (90.91%), and did nail trimming (85.45%). The majority of mothers had some knowledge about *E. histolytica* but little knowledge of the transmission mechanism. Understanding these risk factors can aid in reducing and preventing *E. histolytica* infection. More health education is required for the study to increase awareness of Entamoeba risk factors.

Keywords: Amebiasis, *Entamoeba Histolytica*, Pre-School Children, Risk Factors.

INTRODUCTION

Amebiasis is a parasitic disease of the gastrointestinal tract caused by an anaerobic parasitic protozoan *Entamoeba histolytica* (Rawat et al., 2020) that is widespread, especially in tropical regions and most frequently in inadequate hygiene (Peterson et al., 2011). It infects humans and other primates alike (Schuster & Visvesvara, 2004), causing amebiasis in developing countries. It infects about 50 million people worldwide (Haque & Petri Jr, 2006; Rawat et al., 2020).

The high prevalence rates can be seen in Africa, Mexico, India, and some parts of Central and South America. The infection is increased by poor sanitary conditions, inadequate water, sanitation, and hygiene. Texas and California have significantly higher rates of amebiasis in the U.S., in addition to the rates observed in Asia (Gunther et al., 2011). It is also recognized that *E. histolytica* is a newly discovered sexually transmissible pathogen (Escolà-Vergé et al., 2017). Ac-



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cording to previous studies, co-infection with HIV raises the chance of acquiring *E. histolytica*. Prior research reveals the possibility of infection with *E. histolytica* if a person is also infected with HIV (Hung et al., 2008).

Humans become infected by eating contaminated raw vegetables, any food or drink containing the cyst of *E. histolytica*, and by indirect transmission by the fecal-oral route (Haque et al., 2003). After ingestion, only mature cysts resist the stomach acidity and pass into the small intestines, where an excystation process occurs. Infections can be either asymptomatic or symptomatic infections, which include the ulceration of the wall of the large intestine and amoebic dysentery (intestinal amebiasis). The passage of trophozoites via the portal blood may occur and lead to amoebic liver abscesses and lung abscesses (extra-intestinal amebiasis). As a result, secondary bacterial infection may occur. Bloody diarrhea, weight loss, exhaustion, and stomach pain are some symptoms (Kow-Tong et al., 2001). Diagnosis is established directly by microscopic examination for cysts and trophozoite in the patient's fresh and preserved stool specimens, smears acquired through protoscopy, and drawout of abscesses and other tissue specimens. Microscopy is another laboratory technique used for diagnosis (Walsh, 1986), culture (Clark & Diamond, 2002), serological testing (Ohnishi & Murata, 1997), antibody titers (Gathiram & Jackson, 1987; Jackson et al., 1985; Ravdin et al., 1990), and polymerase chain reaction (PCR) assay (Fotedar et al., 2007). Amebiasis can be effectively treated with several interventions, such as medication, surgery, and preventative measures. The preferred medication for treating amebiasis is nitroimidazole derivatives (metronidazole or tinidazole) (Farthing, 2006).

The prevalence of *E. histolytica* in Libya has been reported in various studies, highlighting its public health significance in the region. Studies have reported varying prevalence rates. For instance, a study conducted in 2014 reported that the prevalence of *E. histolytica* in primary schools in Zawia was 3.1% (Mergani et al., 2014), 3%–4% of *E. histolytica* was found in school children in Tripoli (Kassem et al., 2007), 6.6% in Derna District (Sadaga & Kassem, 2007), 15.7% in Benghazi (El-Boulaqi et al., 1980), and 36.57% among children and neonates in Sirt (Kassem et al., 2007). 3.1% of *E. histolytica* was found in primary school children in Zawia (Elsaid et al., 2014).

The prevalence was slightly higher, 11.8% among children in Zliten, as reported by (Ali et al., 2005). In Khoms, the prevalence of *E. histolytica* is 12.1% among school-aged children and adults (El Ammari & Nair, 2015), while in Brak, Wadi Al Shati, it is 9.5% among adults and children (Mergani et al., 2014).

The study objective was to determine the occurrence of risk factors for *Entamoeba histolytica* infection among children at Qobat Alsakhra, Alqodes, and Alnajah preschools in the western region of Libya.

MATERIALS AND METHODS

The study participants were 55 (27 male and 28 female) aged between 2 and 5. The present study was conducted from March to May 2023 in three preschools involving children in the western region of Libya. A cross-sectional study was undertaken at Qobat Alsakhra, Alqodes, and Alnajah preschools.

A structured questionnaire was created and administered confidentially to each mother participant who agreed to take part, and who provided the following details: age, sex, residence, educational level of mothers, average income, washing hands after defecation, washing hands be-

fore eating, nail trimming, consumption of raw or undercooked meat, source of water, consumption of unwashed fruits, and contact with soil (WHO, 2012). After all questionnaire responses were entered into Microsoft Excel® 2007 (Microsoft Corporation, USA), SPSS Version 21 (SPSS, Inc., Chicago, IL, USA) was used to perform descriptive analysis, while qualitative variables were estimated and displayed as frequencies and percentages. The data containing quantitative variables were expressed as the mean $\pm$ standard deviation ($\pm$ s.d.) and range.

RESULTS

A total of fifty-five (55) children aged from 2 to 5 years were involved in the study. The results showed that 41.82% (23/55) of respondents were from Sabratha, 54.55% (30/55) from Surman, and 3.62% (2/55) from Dahman. The educational level of their mothers showed that 69.09% (38/55) had a bachelor's degree; in contrast, 1.82% (1/55) had a low degree. The results also showed that (54.55%) 30/55 of the respondents had a moderate average income, while the majority had no average income above 1500 d 100% (0/55). Several risk factors for *E. histolytica* were investigated in the survey, and the analysis of data showed that the majority of them, 90.91% (50/55), washed their hands after entering the bathroom. The results also showed that 85.45% (47/55) of respondents trimmed their nails.

The data collected showed 70.91% (39/55) washed their hands before eating and 29.09% (16/55) did not wash their hands. All of them (100%) consumed thoroughly cooked meat (Table 1). The results also showed that 81.82% (45/55) of respondents washed fruits and vegetables before eating them, and 18.18% (10/55) consumed them without washing them.

Regarding contact with soil, results revealed that 87.27% (48/55) of respondents were in contact with soil. All results are shown in Table 1.

About 61.82% (34/55) of respondents drink treated water, 23.64% (13/55) consume mineral water, and 14.55% (8/55) drink from water wells, and all do not consume tap water 0% (0/55) (table 2).

Table (1). Frequency of washing hands after entering the bathroom, nail trimming, hand washing before eating, cooked meats, and washing fruits before eating: (sample size=55)

washing hands after entering the bathroom	Frequency	Percent (%)
Yes	50	90.91%
No	5	9.09%
Nail trimming		
Yes	87	85.45%
No	8	14.55%
Hand washing before eating		
Yes	39	70.91%
No	16	29.09%
Cooked meats		
Well-cooked	55	100%
Half cooked	0	0%
Washing fruits before eating		
Yes	45	81.82%
No	10	18.18%
Contact with soil		
Yes	84	87.27%
No	7	12.73%

Table. (2) Frequency of water sources

Water sources	Frequency	Percentage (%)
Treated water	34	61.82%
Taps water	0	%0
Mineral water	13	23.64%
Wells water	8	14.55%
Total	55	%100

DISCUSSION

Amebiasis is an infection with the intestinal protozoa *E. histolytica*. Children contract the infection by consuming contaminated food or water that contains infectious stages (cysts). Through contaminated food or water supplies, the infection can spread swiftly to other individuals through infected stool. Most of the time, the infection is asymptomatic, but sometimes, if the disease progresses and the parasite invades the lining of the large intestine, bloody diarrhea, abdominal pain, cramping, nausea, and loss of appetite may occur.

This investigation aimed to discover the previous risk factors among preschool children in the western region of Libya using a questionnaire survey. The current study demonstrated that the highest average income (69.09%) was found among mothers who have bachelor's degrees (WHO, 2011). This was because the percentage of mothers' education was simple and reflected their average monthly income. (Hasan et al., 2023) found that low income and education levels are significant factors in the spread of *E. histolytica* among people. The higher the level of awareness and education, the higher the average monthly income.

The lowest rate (9.09%) does not wash their hands after entering the bathroom, mostly in children at the age of 4-5 years, where the transmission of the disease is more common by contaminated hands (Pham Duc et al., 2011) compared to (90.91%) under 2 years of age of children who are still under the care of their mothers.

The study also showed that the majority (70.91%) washed their hands before eating; this result may be due to the health awareness among most mothers. (Rinne et al., 2005) identified contaminated hands as a risk factor for amebiasis infection in children.

Nail trimming due to the high level of education decreases the possibility of transmission of Entamoeba infection. Mostly, 85.45% of children trim their nails regularly, where long nails play an important role in the transmission of some infections. Based on the results, we can note that most Libyans have a high level of health awareness about meat consumption, where 100% of the total consumed is thoroughly cooked meat. A previous study revealed that meat and vegetable food products had high levels of intestinal parasite infestation (Nyarango et al., 2008).

The transmission of Entamoeba infection in children also occurs through eating contaminated vegetables and fruits, where (81.82%) of mothers wash or peel vegetables very well to prevent infection and maintain their children's health.

According to a study, vegetables' high intestinal parasite content may be a common way for Entamoeba infections to spread (Nyarango et al., 2008). (87.27%) of the children are in contact with soil due to their susceptibility to dehydration, *E. histolytica* cysts are unlikely to survive in soil for longer than ten days (Feachem, 1983).

Our study's findings also indicated that treated water was the most widely used (61.82%), which is considered safe for drinking. Also, 0% of them consumed tap water, and therefore, household water sources are one of the potential risks of waterborne infection for humans. This agrees with a study by (Hasan et al., 2023). Additionally, the study showed that 70% of resulting negative respondents were washing their hands after entering the bathroom or washing their hands before eating, 30% of resulting positives were in contact with soil, and regarding water sources, 61.8% of respondents consumed treated water, and 14.55% consumed well water, and 23.64% used mineral water.

CONCLUSION

The prevalence of *E. histolytica* in children remains a significant public health concern, particularly in developing regions. Studies indicate that children, especially those in poor sanitary conditions, are at higher risk of infection due to factors such as inadequate access to clean water, poor hygiene practices, and malnutrition. Efforts to reduce the prevalence should focus on improving sanitation, promoting hygiene education, and ensuring access to clean water. Surveillance and research are crucial for understanding transmission dynamics and developing effective interventions. Addressing these factors can significantly decrease the burden of *E. histolytica* in pediatric populations and improve overall child health outcomes.

RECOMMENDATIONS

Additional research is recommended to determine the prevalence of *E. histolytica* among children, and further investigations using modern and more sensitive techniques, such as PCR, are needed. In addition, according to the study, public health education is essential to increasing knowledge of *E. histolytica* infection.

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ETHICS

The study obtained ethical approval from the directors of preschools.

Duality of interest: The authors declare that they have no duality of interest associated with this manuscript.

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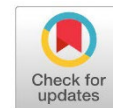
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Research Article

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The Impact of Phototherapy on a Term Newborn's Blood Calcium Level at Al-Bayda Medical Center, Libya

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Abstract

During the first week of birth, the most prevalent abnormal physical finding is Neonatal Hyperbilirubinemia (NH). Phototherapy is important in both the prevention and treatment of hyperbilirubinemia. However, there's a chance that this therapeutic approach may have unintended consequences. The purpose of this study was to ascertain how phototherapy affected the serum calcium levels of term neonates with unconjugated hyperbilirubinemia. 50 newborns undergoing phototherapy who were admitted to the Neonatal Intensive Care Unit were the subjects of a prospective hospital-based observational study. Serum levels of calcium and bilirubin were measured both before and after phototherapy ended. The initial samples served as the reference points. The mean gestational age was 37.02 ± 0.25 weeks, and the mean birth weight was 3.21 ± 0.45 kg. The average phototherapy session lasted 39.36 ± 11.64 hours. Phototherapy significantly lowered serum calcium levels with the mean before phototherapy being 8.89 ± 0.99 SD and after 8.14 ± 1.22 SD, $p < 0.001$. Hypocalcemia developed in 32 (64%) babies, among them 16 (32%) had a calcium deficiency before phototherapy. The study concluded that phototherapy had a considerable impact on calcium levels in a term neonate with hyperbilirubinemia.

Keywords: Hyperbilirubinemia, Jaundice, Phototherapy, Full-term, Neonate, Hypocalcaemia.

INTRODUCTION

Jaundice is a yellow coloring of the skin, sclera, and other body tissues caused by the deposition of bilirubin in cases of hyperbilirubinemia when the bilirubin level exceeds 2 mg/dl or 34.2 $\mu\text{mol/l}$ (Abbas et al., 2016). Jaundice is observed during the 1st week of life in approximately 60% of term neonates and 80% of pre-term neonates. Jaundice from the deposition of indirect bilirubin (non-obstructive jaundice) in the skin tends to appear bright yellow or orange. Infants with severe hyperbilirubinemia may present with lethargy and poor feeding and, without proper management, can progress to acute bilirubin encephalopathy (Kernicterus) (Carter & Feigelman, 2020). It has also been studied that unconjugated hyperbilirubinemia reflects normal or exaggerated physiological phenomena, mostly in neonates (Singh, 2017). Phototherapy changes the structure of bilirubin and thus increases its excretion, which is the standard treatment for neonatal jaundice (Faulhaber et al., 2019).



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One of the findings observed in some studies during phototherapy is hypocalcemia, defined as a total blood calcium level of less than 8 mg/dl (2 mmol/l) in term neonates. However, the results of these studies were not conclusive. Hypocalcemia during phototherapy might be caused by transcranial light inhibiting the pineal gland, leading to decreased melatonin levels.. So, when melatonin level is decreased hypocalcemia develops (Alizadeh-Taheri et al., 2013). The purpose of this study was to assess the prevalence of and contributing variables to hypocalcemia in full-term neonates receiving phototherapy.

PATIENTS AND METHODS

Study population and setting: A total of 50 full-term neonates were delivered in Al-Bayda Medical Center, Al-Bayda, Libya, from June 2021 to January 2022.

Data collection: A special data collection sheet was designed for this study which includes family name, age, sex, mode of delivery, gestational age, perinatal and natal history, family history, maternal illness, onset of jaundice, duration of phototherapy, weight, length. Systemic examination for signs of hypocalcemia after phototherapy, like Jitteriness, apnea, and convulsion, as well as investigations which include: TSB, S. Ca before and after phototherapy.

Inclusion criteria: All term, normal jaundiced infants undergoing phototherapy were included in this study with S .bilirubin above 15 mg/dl.

Exclusion criteria: Pathological jaundice, preterm, asphyxia, infant of a diabetic mother, hypothyroidism, sepsis, IUGR, congenital malformation. Mothers received drugs: such as phenobarbital, Mg sulfate, and oxytocin, and infants received blood exchange.

Study design: prospective study.

Study setting: The Neonatal Unit in Al-Bayda Medical Center, which is a part of the Pediatric Department. It contains 18 incubators connected to a central oxygen supply and 15 baby cots, 3 mechanical ventilators, 5 CPAP machines, 6 phototherapy machines, 6 monitor machines for monitoring vital signs, one cylindrical phototherapy, and 2 radiant warmers. The unit is staffed by one resident doctor on duty and two nurses.

Study period: from June 2021 to January 2022.

Sample: the study sample included (50) neonates.

Statistical analysis: The statistical package for social science software (SPSS) was used to analyze the acquired data statistically. Variables that adhered to a normal distribution were summed up as mean and standard deviation. The independent sample t-test and the chi-square test were employed to compare the two groups. Numbers and percentages were used to present qualitative data. It was thought to be statistically significant at $p < 0.05$.

Limitations: The level of ionized calcium was not included in the study because it was unavailable.

RESULTS

A total of fifty cases meeting the inclusion/exclusion criteria were enrolled in this study. Their

ages ranged from 2 - 12 days with a mean of 5.48 ± 2.74 SD. 22 (44%) were male whereas 28 (56%) were females. Their weights ranged from 2.5-4.2 kg with a mean of 3.21 ± 0.45 SD. Gestational age was between 37-38 weeks with a mean of 37.02 ± 0.25 SD, and the mean of the babies' height was 47.44 ± 0.54 SD (Table 1).

Table (1). Distribution of babies according to demographic characteristics

Demographic Characteristic	Age/days	Weight/kg	Height/cm	# GA/weeks
Min	2	2.5	47	37
Max	12	4.2	49	38
Mean $\pm$ SD	5.48 ± 2.74	3.21 ± 0.45	47.44 ± 0.54	37.02 ± 0.25
Median	5	3	47.5	37

GA = gestational age

29 (58 %) of them were delivered vaginally (Figure 1). The onset of jaundice was between 2-5 days with a mean of 2.62 ± 0.75 SD, and no cases were recorded in the first 24 hours. The duration of phototherapy was 24-48 hours, mean of 39.36 ± 11.64 SD (Table 2).

Table (2). Distribution of babies according to onset and duration of phototherapy

Variable	Onset of jaundice/days	Duration of photo/hrs.
Min	2	24
Max	5	48
Mean $\pm$ SD	2.62 ± 0.75	39.36 ± 11.64
Median	2.5	36

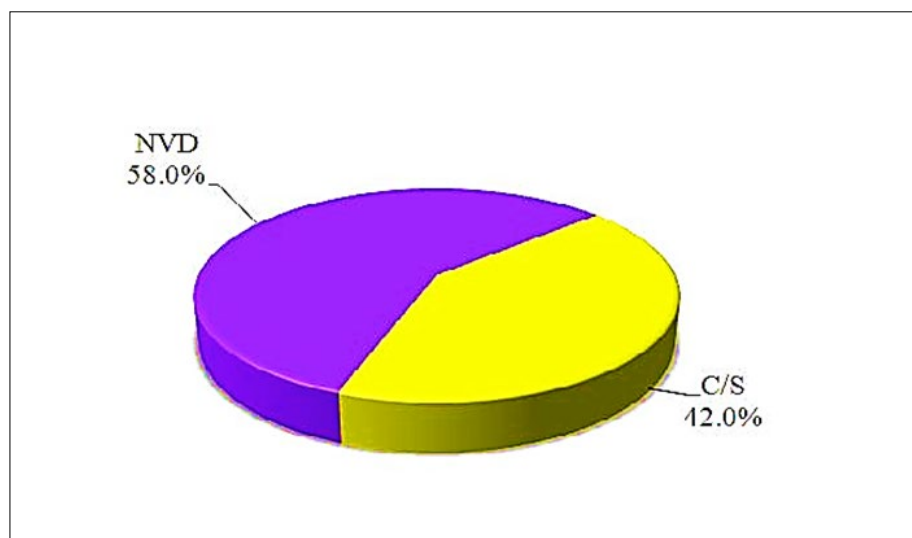


Figure (1). Distribution of babies according to mode of delivery

The serum bilirubin levels ranged from 15-18mg/dl with a mean of 16.72 ± 1.41 SD before phototherapy, and 4-11mg /dl with a mean of 8.87 ± 1.71 SD after phototherapy, and there was a significant drop in serum bilirubin $p < 0.001$ (Table 3).

Table (3). Distribution of the babies according to TSB mg/dl.

TSB	Before photo	After photo	T	p
Min	15	4		
Max	18	11		
Mean $\pm$ SD	16.72 $\pm$ 1.41	8.87 $\pm$ 1.71	32.384	P<0.001
Median (IQR)	16.8	9.5		

t: paired t-test

There is a significant association between phototherapy and a drop in serum calcium levels with a mean of 8.89 ± 0.99 SD before phototherapy and a mean of 8.14 ± 1.22 SD after phototherapy. 32 (64%) of the babies developed hypocalcemia after phototherapy and among them, 16 (32%) had a deficiency in calcium before phototherapy. 4/32 babies developed symptoms of hypocalcemia, one convulsion, one irritability, and 2 developed jitteriness. Statistical analysis shows a significant association between phototherapy and a drop in serum calcium level with $p = 0.00$ (Table 4). In contrast, 1(2%) developed hypercalcemia after phototherapy.

Table (4). Distribution of the babies according to S. Ca.

S. Ca mg/dl	Before photo		After photo		T	P
	NO	%	No	%		
4-8	18	36	32	64		
8-11	31	62	17	34	t=8.321	0.001
>11	1	2	1	2		

Of babies who developed hypocalcemia, 53% were female, and only one female patient developed hypercalcemia. Statistical analysis shows no significant association between gender and changes in serum calcium $P=0.914$ (Table 5).

Table (5). Correlation between S. Ca after phototherapy and gender

S. Ca mg/dl	Male		Female		Total
	NO	%	NO	%	
4-8	15	46.2%	17	53.1%	32
8-11	7	41.9%	10	58.8%	17
>11	0	0.0	1	100	1

$P=0.914$

DISCUSSION

A suitable and secure way to lower a newborn's indirect bilirubin level is through phototherapy. The link between phototherapy and hypocalcemia in newborns was initially proposed by (Romagnodi et al., 1979).

In the studied groups, the mean total serum bilirubin (TSB) was 16.72 ± 1.41 SD, compared to a study by (Karamifar et al., 2002). which showed 18.0 ± 2.4 SD, and (Alizadeh-Taheri et al., 2013), where the mean TSB was 20.1 ± 3.3 SD. The duration of phototherapy was between 24 and 48 hours (39.36 ± 11.64 SD), in contrast to the (Eghbalian & Monsef, 2002), where it was 3 days.

After phototherapy, 32(64%) individuals in our study were hypocalcemia which is statistically

significant $p < 0.001$. The study by (Karamifar et al., 2002). was correlated with the current study with the significant decrease in serum calcium levels reported in term newborns following phototherapy. In premature neonates, (Romagnodi et al., 1979) were the first to propose a link between hypocalcemia and phototherapy in 1979, and they found hypocalcemia in 52.3% of newborns. According to (Sethi et al., 1993) 75% of full-term newborns developed hypocalcaemia after phototherapy. These studies support the findings of the current study.

Correlation of hypocalcemia with other studies

Study	Year	No. of participants	Hypocalcemia after photo	P
Sethi et al.	1993	40	75%	$p < 0.05$
Jain et al.	1998	40	30%	$p < 0.05$
Karamifar et al.	2002	153	8.7%	$p < 0.018$
Yadav RK et al.	2012	30	66.6%	$p < 0.05$
Arora et al.	2014	100	56%	$P < 0.05$
Our study	2022	50	64%	$p < 0.001^{**}$

(Jain et al., 1998), following phototherapy, 30% of full-term newborns experienced hypocalcemia. In (Dutta, 2001) findings, phototherapy caused hypocalcemia in 75% of full-term infants. (Karamifar et al., 2002) reported that the prevalence of hypocalcemia in full-term infants was 8.7% ($p = 0.018$). (Eghbalian & Monsef, 2002) study discovered a statistically significant difference ($p < 0.05$) between serum calcium levels before and after phototherapy. Romagnoli, C. 1979, Phototherapy-induced hypocalcemia. *Journal of Pediatrics*, 94: 815-816. (Yadav et al., 2012) study following 48 hours of phototherapy, 66.6% of term neonates developed a decrease in their calcium levels $p < 0.05$. (Alizadeh-Taheri et al., 2013) studied the prevalence of phototherapy-induced hypocalcemia in 147 term neonates and found a decrease in serum calcium levels in 56% of babies out of which 7% developed significant hypocalcemia ($p = 0.03$) after 48 hours of phototherapy.

(Arora et al., 2014) study concluded that hypocalcemia was more frequently observed in term neonates. A much higher incidence of hypocalcemia was observed by (Sethi et al., 1993) and the lowest incidence was reported by (Karamifar et al., 2002). The reason for this difference is not clear but can be explained by the lower number of study groups taken in the other studies.

In our study, hypocalcemia occurred more frequently after 48 hrs of continuous phototherapy which was similar to the (Arora et al., 2014). Symptomatic hypocalcemia was observed in (Arora et al., 2014; Jain et al., 1998; Sethi et al., 1993) In the present study, it was observed that phototherapy induces a considerable decline in serum calcium levels in icteric newborn therapy. This decline may continue down to the threshold of hypocalcemia and be accompanied by signs and symptoms of hypocalcemia such as jitteriness, apnea, irritability, and or convulsion which was in comparison to the (Karamifar et al., 2002) study.

Comparison of mean serum calcium levels before and after phototherapy in term neonates with other studies

Study	Mean $\pm$ SD serum calcium Level		p-value
	Before phototherapy	After phototherapy	
Eghbalian et al.	9.85 $\pm$ 1.23	9.09 $\pm$ 0.93	< 0.001
Karamifar et al.	9.53 $\pm$ 0.92	9.30 $\pm$ 1.11	0.043
Taheri et al.	9.8 $\pm$ 0.80	9.5 $\pm$ 0.90	< 0.05
Our Study	8.89 $\pm$ 0.99	8.14 $\pm$ 1.22	$< 0.001^{**}$

In our study, there was a significant decline in mean serum calcium levels following phototherapy in term neonates, also ($p < 0.001$) which was similar to the other studies done by (Alizadeh-Taheri et al., 2013; Eghbalian & Monsef, 2002; Karamifar et al., 2002).

CONCLUSION

Among newborns treated with phototherapy who are jaundiced, hypocalcemia is a common occurrence. When working with newborns in this situation, we should be mindful that institutional policy and research priorities should take serial monitoring for hypocalcemia and its consequences into account.

Our study explains the significant effect of phototherapy on calcium levels in term neonates (64%) with jaundice receiving phototherapy. The range of ca was < 8.5 mg/dl. Although the signs were not remarkable, some infants developed complications like convulsions, jitteriness, and irritability.

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ETHICS

Informed consent was obtained from the patient's parents regarding the study objectives and methods.

Duality of interest: Yes, there is a conflict of interest in this manuscript.

Author contributions: A. developed the theoretical formalism. B supervised the project. A, C, and D performed the analytic calculations and performed the numerical simulations. All authors read, reviewed, and approved the final manuscript

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Research Article

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Exploring the Side Effects and Drug-Drug Interactions Resulting from Polypharmacy: A Case Study from Cardiovascular Pharmacotherapy



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Abstract

In clinical practice, it is standard procedure to assess potential drug-drug interactions (DDIs) when prescribing multiple medications to a single patient. The prevalence of DDIs escalates with an increased number of concurrently prescribed drugs. Polypharmacy, as defined by the World Health Organization, entails the administration of numerous medications simultaneously, or an excessive number of medications. We postulate a close association between polypharmacy and DDIs. This study presents a singular case investigation encompassing a comprehensive review of all prescribed and over-the-counter medications, medical history, and laboratory results, coupled with an extensive cross-referencing with existing literature to identify DDIs associated with polypharmacy. Our findings underscore a robust positive correlation between polypharmacy and DDIs, with a total of 83 documented instances. Notably, antibiotics emerged as the medication class responsible for the highest number of DDIs, accounting for 13 cases.

Keywords: Drug-drug interactions, Polypharmacy, Drug Side Effects, Case Study.

INTRODUCTION

Drug-drug interactions (DDIs) refer to adverse effects that arise when two medications are concurrently administered to the same patient (Seymour & Routledge, 1998). These interactions can occur through various mechanisms and range from mild effects that may not require adjustments to high-risk situations where modification or cessation of one medication is necessary.

While adding a medication is typically intended to improve a patient's health, it also increases the potential for DDIs and drug-disease interactions. Clinically significant DDIs can manifest as reduced therapeutic effects of a drug, increased occurrences of adverse drug reactions, and compromised treatment outcomes (Hines & Murphy, 2011). Severe DDIs are those that pose life-threatening risks or necessitate medical intervention to minimize or prevent severe adverse effects.

Polypharmacy encompasses the prescription of more medications than typically recommended in the literature, often exceeding six drugs concurrently (Johnell & Klarin, 2007). Specifically, polypharmacy is defined as the simultaneous use of five or more medications, while hyperpolypharmacy denotes the concurrent use of ten or more medications (Masnoon et al., 2017). The



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prevalence of polypharmacy varies across different populations and tends to rise with age. In a comprehensive study involving 1,742,336 older adults, polypharmacy affected 44% of the population (Khezrian et al., 2020). According to Scottish Polypharmacy Guidance, up to 11% of unplanned hospital admissions were linked to adverse effects stemming from polypharmacy, with approximately 50% of these incidents deemed preventable (Khezrian et al., 2020). Furthermore, a prospective study of 5052 older adults in Spain concluded that polypharmacy was associated with nearly a 1.8 times higher risk of mortality (Gómez et al., 2015).

Cardiovascular disease (CVD) is a group of disorders affecting the heart and blood vessels, including coronary heart disease, cerebrovascular disease, hypertension, peripheral arterial disease, heart failure, and arrhythmias. According to the American Heart Association (AHA), the incidence of CVD in the US is approximately 75% among individuals aged 60 to 79 years and rises to 86% among those aged 80 and older (Yazdanyar & Newman, 2009). Evidence-based practice for treating CVD typically involves using combinations of medications tailored to specific diseases (Fleg et al., 2011). Consequently, polypharmacy and potential drug-drug interactions (DDIs), along with their associated consequences, are common among older adults with CVD.

Many treatment regimens for cardiovascular conditions require prescribing multiple medications simultaneously, targeting various organs and necessitating multifaceted treatment approaches. For instance, congestive heart failure (CHF) affects organs such as the lungs, kidneys, and liver, with medication regimens aimed at preventing complications and enhancing quality of life. Depending on the disease stage and individual condition, patients with CHF may be prescribed up to eight medications (AHA). Moreover, CHF patients often present with concurrent conditions that require separate treatment, further increasing the complexity and number of medications administered. In such cases, the side effects of one medication may be mistaken for signs or symptoms of another condition, potentially leading to additional prescriptions.

Considering these factors, polypharmacy in cardiovascular medicine may indeed, elevate the incidence of drug-drug interactions (DDIs) and compromise the overall quality of life for patients. The simultaneous use of multiple medications in the treatment of cardiovascular diseases increases the complexity of managing potential interactions between drugs. These interactions can range from mild to severe, impacting the effectiveness of treatment and potentially leading to adverse effects or reduced therapeutic outcomes.

Furthermore, polypharmacy can contribute to medication adherence challenges and increase the risk of adverse drug reactions, particularly in older adults who may be more vulnerable due to age-related physiological changes and comorbidities. The need for careful monitoring and management of medication regimens is crucial to minimize the risks associated with polypharmacy in cardiovascular care.

In summary, while polypharmacy is often necessary to address the multifaceted nature of cardiovascular conditions, healthcare providers must remain vigilant in assessing and mitigating the risks of drug interactions to optimize patient outcomes and maintain quality of life.

MATERIALS AND METHODS

Hypothesis

Polypharmacy has the potential to precipitate serious complications, resulting in an escalation of prescribed medications and subsequent drug-drug interactions. This cascade can exacerbate existing

health issues, introduce additional complications, and potentially contribute to the onset of new medical conditions.

Methods

This study is a single case investigation involving a comprehensive review of the patient's medication record, encompassing approximately 32 prescriptions and over-the-counter (OTC) medications. The aim is to thoroughly analyze potential polypharmacy issues and their associated consequences, including drug-drug interactions, undertreated or overtreated conditions, and contraindications.

To identify the most prevalent drug-drug interactions and understand their pharmacological mechanisms, references from authoritative sources were consulted. The following texts and applications were utilized:

- Martindale: The Complete Drug Reference. 37th edition, edited by Sean C Sweetman.
- The British National Formulary (BNF). 69th edition. British Medical Association and Royal Pharmaceutical Society, 2015.
- Medscape drug-drug interactions checker.
- Drugs.com drug-drug interactions checker.

These resources were selected for their reliability in providing up-to-date information on pharmacological interactions and guidelines for medication management.

Case Presentation

HA, an 84-year-old female, presented with multiple intermittent complaints, including swelling of the lower limbs limiting daily movement, muscle pain and cramps, dizziness, fatigue, vomiting, nausea, vertigo, hearing loss, difficulty swallowing, persistent cough, and trouble breathing. She had no history of diabetes or hypertension.

Patient's Medical History

- **History of Most Recent Illnesses:**
 - o Pneumonia with pleural effusion
 - o Lower limb edema
 - o Asthma
 - o Cardiomyopathy (conflicting data regarding ischemic heart disease)
 - o Dehydration
 - o Renal artery spasm
- **Past Medical History:**
 - o Rheumatoid arthritis with leukocytoclastic vasculitis (LCV) since 1992
 - o Old infarctive cerebrovascular accident (CVA or stroke)
 - o Secondary epilepsy due to CVA on January 26, 2013
 - o Kidney stones: underwent left kidney shock wave lithotripsy (SWL)
 - o Surgical: bilateral total knee replacement

Patient's List of Medications

Table: (1). List of drugs used by the patient under study

Brand Name	Generic Name	Duration/ Time
Nexium 40mg	Esomeprazole	Long Term Use
Aspirin 75mg	Acetyl Salicylic Acid	Long Term Use
Vastarel MR 35mg	Trimetazidine	Long Term Use
Carvedilol 6.25mg	Carvedilol	Long Term Use
Lasix 40mg	Furosemide	Long Term Use
Spironolactone 25mg	Spironolactone	Long Term Use
Atorvastatin 10mg	Atorvastatin	Long Term Use
Bisacodyl 5mg	Bisacodyl	Long Term Use
Madopar 125mg	Levodopa/carbidopa	Long Term Use
Allopurinol 300mg	Allopurinol	Long Term Use
Perindopril 5mg	Perindopril	Alternating with lisinopril
Lisinopril 5mg	Lisinopril	Alternating with Perindopril
Depakine Chrono 500mg	Sodium valproate	Long Term Use
Kaleorid 600mg	Potassium chloride	Long Term Use
Gemifloxacin	Gemifloxacin	13/4/2016
Bisolvon syrup	Bromhexine	13/4/2016
Clarithromycin 500mg	Clarithromycin	12/12/16
Trifid tablet	Triprolidine/pseudoephedrine	12/12/16
Night nurse syrup	Promethazine HCL/paracetamol/dextromethorphan/ ethanol alcohol	12/12/16
Rocephin IM inj.	Ceftriaxone	12/12/16
Gemifloxacin	Gemifloxacin	20/12/2016
Rapidos 50mg	Diclofenac potassium	20/12/2016
Levofloxacin 750mg	Levofloxacin	23/4/2017
Mucosolvon syrup	Ambroxol HCl	23/4/2017
Ventolin nebulizer	Salbutamol	23/4/2017
Pulmicort nebulizer	Budesonide	23/4/2017
Seroflo 250/5mg	Salmeterol/fluticasone	23/4/2017
Avamys nasal spray	Fluticasone furoate	30/4/2017
Aerius Syrup	Desloratadine	30/4/2017
Betaserc 16mg	Betahistine HCL	30/4/2017
B-comp syrup	Vitamin B Supplement	30/4/2017
Motilium 10mg	Domperidone maleate	15/5/2017
Cortigen B6 inj.	Pyridoxine and suprarenal cortex extract	15/5/2017

RESULTS AND DISCUSSION

After a comprehensive analysis of potential polypharmacy and drug-drug interactions, the results confirm varying definitions of polypharmacy, often defined as exceeding the upper limit of concurrent medications, typically more than six drugs. This study identified instances of unnecessary medications, drug-drug interactions (DDIs), drug-disease interactions, and exacerbation of the patient's medical condition, necessitating additional prescriptions to manage complications possibly induced by unstudied medication combinations. This cascade effect contributed to an escalation in both the quantity and adverse effects of prescribed medications.

All identified DDIs were categorized based on their impact on exacerbating the patient's condition.

DDIs Resulting in Inappropriate Treatment Indications

Trimetazidine-induced Parkinson-like Syndrome: Trimetazidine, a metabolic agent, affects glucose metabolism and is used to protect against myocardial ischemia. Following a safety review by the European Medicines Agency on June 21, 2012, concerns were raised about its effectiveness and

reports of movement disorders resembling Parkinson's symptoms. The Committee for Medicinal Products for Human Use (CHMP) concluded that while the benefits outweigh the risks in patients with angina pectoris, treatment should be restricted to add-on therapy for patients inadequately controlled by or intolerant to other angina treatments. In this case, the addition of Trimetazidine led to six additional drug-drug interactions after the patient developed Parkinsonian symptoms and required treatment with Madopar.

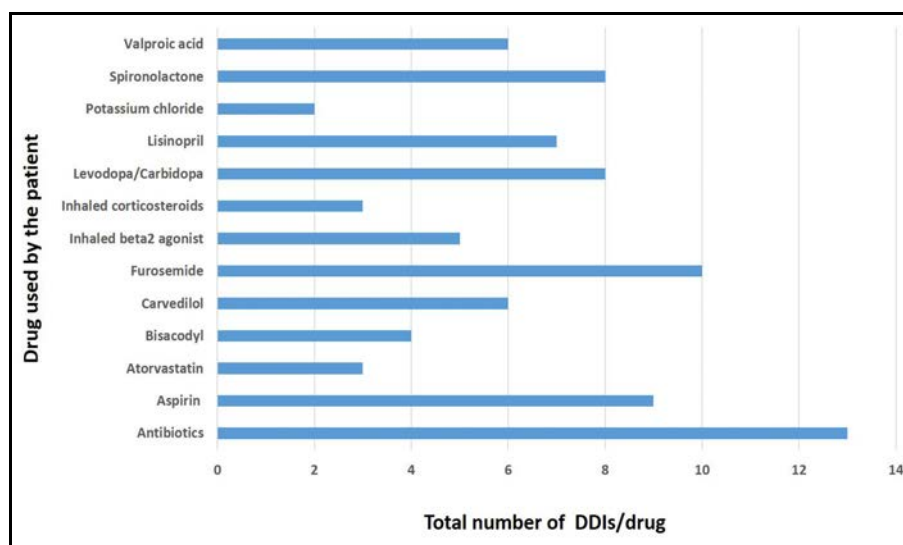


Figure: (1). Number of drug-drug interactions caused by each drug used by the patient.

DDIs Resulting in Therapeutic Failure: Beta2 Agonists and Non-Selective Beta Antagonists

Beta-blockers can antagonize the effects of beta-2 adrenergic bronchodilators, potentially precipitating acute, life-threatening bronchospasm in patients with asthma or other obstructive airway diseases. This drug-drug interaction (DDI) resulted in five prescriptions, multiple hospital visits, and trials of five respiratory antibiotics, which collectively contributed to thirteen DDIs. One of these interactions posed a major risk, involving substantial consequences. Additionally, trials of two different inhaled beta2 agonists introduced five more DDIs, while the use of three inhaled corticosteroids added approximately three additional DDIs. Over-the-counter cough remedies combining antihistamines exacerbated this issue, leading to synergistic sedative effects and nine additional DDIs. Lastly, a trial of Desloratadine, intended for vertigo and hearing loss, antagonized Betahistine, the recommended treatment for these conditions.

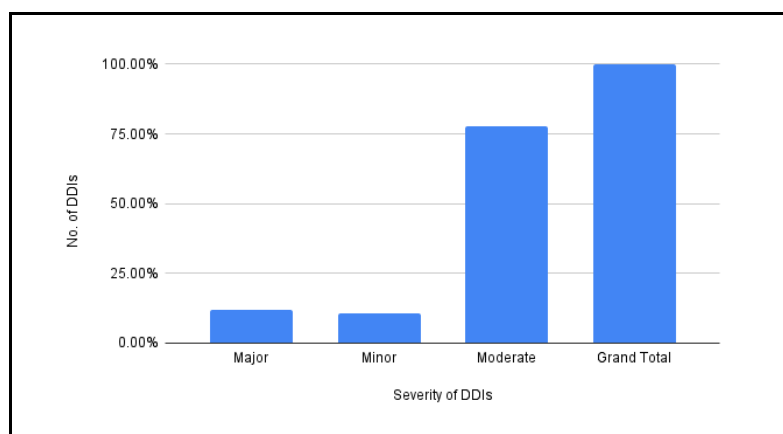


Figure: (2). Number of DDIs versus their severity as a percentage of the grand total of DDIs

DDIs Contributing to Statin-Induced Myalgia: Atorvastatin, Clarithromycin, and Esomeprazole

Certain macrolide antibiotics such as troleandomycin, erythromycin, and clarithromycin inhibit the enzyme CYP450 3A4. This inhibition can lead to elevated plasma concentrations of HMG-CoA reductase inhibitors (statins) metabolized by this isoenzyme, potentially contributing to statin-induced myalgia.

This revision clarifies the relationship between macrolide antibiotics and statin metabolism, highlighting how these interactions may affect patient outcomes, particularly in terms of myalgia associated with statin therapy.

DDIs Resulting in QT Interval Prolongation:

- Antibiotics: levofloxacin, gemifloxacin, and clarithromycin.
- Beta2 agonists: salmeterol and albuterol.
- Bisacodyl.
- Furosemide.
- Promethazine.

DDIs Adversely Affecting Renal Function:

- **Hyperkalemia:** Caused by the combination of Spironolactone, ACE inhibitors (ACEIs), and Potassium Chloride. Concurrent use of Spironolactone and potassium supplements can lead to severe and life-threatening hyperkalemia.
- **Hyperuricemia:** Induced by the combination of Furosemide, Levodopa, and low-dose salicylates. Hyperuricemia can manifest as an asymptomatic condition characterized by elevated serum uric acid levels, with a urate concentration above 7.0 mg/dl indicating an increased risk of gout. Diuretics, salicylates, and levodopa, all taken concurrently by our patient, can reduce uric acid clearance through various mechanisms. Test results from 2016 showed a significant increase in serum urea, exceeding the upper limit by three-fold in October 2016. By April 2017, urea levels remained elevated, accompanied by an increase in uric acid to 10.5 mg/dl. Discontinuation of furosemide resulted in improved renal function, with subsequent tests in May 2017 revealing reduced urea levels to 61 mg/dl and uric acid levels to 8.14 mg/dl, confirming furosemide's contribution to elevated serum uric acid levels.

DDIs Resulting in Central Nervous System Adverse Drug Reactions: Valproic Acid and Aspirin

- Salicylates, particularly aspirin, have been implicated in displacing valproate from protein-binding sites and inhibiting its clearance. This interaction can lead to a four-fold increase in the free fraction of valproate, potentially amplifying therapeutic and toxic effects. The risk of this interaction is heightened with large or prolonged doses of salicylates, particularly in children.

DDIs resulting in unwanted additive effects:

- Additive lowering in blood pressure; hypotension: Concomitant administration of:
 - o Furosemide + spironolactone + carvedilol + levodopa + promethazine.
 - o Furosemide + spironolactone + carvedilol + lisinopril + promethazine.

CONCLUSION

The results demonstrate an undeniably strong positive correlation between polypharmacy and drug-drug interactions. This connection is primarily influenced by the following factors:

1. The increasing number of drugs and their pharmacological interactions.
2. Prolonged treatment durations without adequate follow-up and monitoring.
3. Use of over-the-counter (OTC) medications without medical advice.
4. Multiple physicians managing distinct medical conditions simultaneously without coordination.
5. Insufficient collaboration among healthcare team members in medication documentation and patient file updates.

These factors collectively contribute to the complexity and risks associated with polypharmacy, highlighting the critical need for improved medication management practices and interdisciplinary communication within healthcare settings.

It can be inferred that with each additional medication, the possibility of drug-drug interactions increases. Logically, these medications are taken by the same person, sharing the same metabolic environment and exerting their effects on interconnected physiological systems within the body. Therefore, medications taken concurrently are pharmacologically connected.

Based on the results, it is recommended to implement stringent guidelines for checking drug-drug interactions before dispensing medications. The severity and detrimental effects of these interactions on the patient's condition should always be evaluated. Many of the mentioned drug-drug interactions could potentially be avoided through monitoring, risk assessment, and evaluating the necessity and true indication of each prescribed medication.

Establishing stronger communication and collaboration between physicians and pharmacists may help mitigate discrepancies in medication regimens, reduce the prevalence of drug-drug interactions, and ultimately enhance the overall quality of life for patients.

Contribution: This research contributes to the understanding of the relationship between polypharmacy and drug-drug interactions (DDIs) by demonstrating a strong positive correlation between the two. Through a detailed case study, the research highlights the significant prevalence of DDIs in patients subjected to polypharmacy as a result of treating cardiovascular diseases, with antibiotics identified as the most frequent contributors to these interactions. This study highlights the importance of careful medication management and monitoring in patients receiving multiple drugs to mitigate the risk of DDIs.

Conflict of interest: The authors declare they have no conflict of interest related to this study. All authors have reviewed and approved the final version of the manuscript, and there are no financial, personal, or professional relationships that could be perceived as influencing the research or its outcomes.

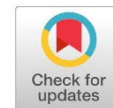
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Research Article

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Breast Cancer and Early Screening Among Female Teachers in Misurata: Evaluating Awareness and Practices

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Abstract

Breast cancer is the most common cancer in women in the Eastern Mediterranean region, and the first or second leading cause of cancer-related deaths among females. The study aimed to evaluate the level of knowledge, attitudes, and practices (KAP) of female teachers in Misurata City, Libya, regarding breast cancer risk factors, signs and symptoms, and screening methods. A cross-sectional study was conducted through a web-based validated questionnaire; 430 responses were received. Data analysis was performed using SPSS v26. 60.5% of participants exhibited a low level of knowledge regarding risk factors, about (73.3%) revealed an excellent level of knowledge concerning breast cancer signs and symptoms, and more than half (53.0%) had a low level of knowledge about breast cancer screening. About 65% of participants exhibited a positive attitude towards breast cancer screening, (65.1%) frequently practice breast cancer screening. Although women in Misurata City have a positive attitude toward breast cancer screening, their poor knowledge hinders them from adopting proper practice techniques. This suggests a need to provide more awareness programs for Libyan women to improve their breast cancer knowledge and practice.

Keywords: Breast Cancer, Breast Cancer Risk Factors, Breast Cancer Screening, Misurata, Libya, Teachers.

INTRODUCTION

In 2022, over 2.3 million cases of breast cancer (BC) were diagnosed, leading to 670,000 deaths worldwide (WHO, 2024). BC ranks as the top or second leading cause of cancer-related deaths in 95% of countries, with low- and middle-income nations contributing to 80% of deaths (WHO, 2023). Data on BC in Libya is limited, but a survey in Misurata reported a cancer incidence of 71.7 per 100,000 people, with BC accounting for 19.5% of cases (Zarmouh et al., 2022). Key BC risk factors include female gender (99% of patients are women), advancing age, obesity, family history, reproductive factors, and smoking. Notably, 50% of cases occur in women without clear risk factors beyond gender and age (Harvie et al., 2015; WHO, 2024). The most common early sign of BC is a painless lump or thickening in the breast. Other symptoms can include changes in breast size or shape, dimpling or redness of the skin, changes in nipple appearance, and abnormal or bloody discharge. These symptoms may become more noticeable as BC progresses (WHO, 2024).



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While screening cannot prevent BC, early detection through mammography reduces mortality by 20-25% (Centers for Disease Control and Prevention (CDC, 2024; Fancellu et al., 2019). However, BC screening in Libya remains limited, with most cases diagnosed at advanced stages (IGRC, 2024). This study assesses BC knowledge, attitudes, and practices among female teachers in Misurata, aiming to link these factors with socio-demographics and improve awareness

MATERIALS AND METHODS

This cross-sectional study, conducted from June 1 to October 1, 2023, aimed to assess the knowledge, attitudes, and practices of female teachers in Misurata City regarding breast cancer and screening. Data were collected via digital questionnaires distributed through social media platforms (WhatsApp, Facebook, Instagram) to female teachers from various schools. A 400-sample size was calculated, with 450 questionnaires distributed and 430 valid responses analyzed. The pre-coded questionnaire had six sections: sociodemographic data (5 questions), knowledge of breast cancer risk factors (5 questions), screening and early detection (16 questions), signs and symptoms (5 questions), attitudes toward screening (10 questions), and screening practices (5 questions). Knowledge was assessed on a binary scale, with correct answers scored as 1 and incorrect answers as 0. The overall knowledge score was categorized as low (<50% correct), moderate (50%-75%), and high (>75%). Knowledge of breast cancer signs and symptoms was determined by scores of 3 or more out of 5. Attitudes were classified as negative (<30% score), neutral (30%-60%), or positive (>60%). Practices were evaluated from no practice (score = 0) to consistent practice (score = 4-5).

Data analysis was conducted using the (IBM.SPSS) V26, and descriptive analysis in the form of frequencies, means, and standard deviations was calculated. Chi-squared test was used to assess the associations between variables, a P -value ≤ 0.05 was considered statistically significant at a confidence level of 95%.

RESULTS

Socio-demographic characteristics

The study enrolled a total of 430 participants, 85.2% of whom were less than 46 years old. Among the participants, 64.2% were university graduates, 8.8% had higher education. 59.5% were married. A family history of (BC) was documented in 15% of participants, whereas only 3.3% had a personal history of (BC). (Table 1).

Table 1 Socio-demographic characteristics of participants (N= 430)

Characteristics		Frequency	Percent
Age, (years)	Less than 35	183	42.6
	36-45	183	42.6
	46-55	45	10.5
	Older than 56	19	4.4
Educational level	High school	59	13.7
	University	276	64.2
	Higher education	37	8.8
	Other	57	13.3
Marital status	Married	256	59.5
	Single	126	29.3
	Other	45	10.5
Family history	Yes	64	15
	No	364	85
History of breast cancer	Yes	14	3.3
	No	416	96.7

Breast cancer knowledge:

1) Breast cancer risk factors

The mean score for knowledge of (BC) risk factors was 6.9 (± 3.6). Most participants (60.5%) had low knowledge, 32.1% had moderate knowledge, and only 6.3% had high knowledge. Regarding specific risk factors, 66.3% and 61.9% of participants incorrectly believed that not breastfeeding and using oral contraceptives were major risk factors. Familial predisposition and unhealthy habits were identified by 59.5%. Additionally, 53.5% and 54.9% believed prolonged use of tight bras and breast imaging respectively linked to (BC). However, only 36.5% recognized sleep disorders and lack of exercise as risk factors.

For reproductive factors, only 21.6%, 37.7%, 30.5%, and 18.8% correctly identified early menarche, late menopause, nulliparity, and late first pregnancy respectively, as risk factors. Moreover, 28.8% and 24.2% identified post-menopausal obesity and large breasts as risks, and 33.0% acknowledged advancing age, (Table 2).

No significant associations were found between BC risk factor knowledge and education ($P = 0.356$), family history ($P = 0.952$), personal history ($P = 0.966$), or marital status ($P = 0.073$). However, a significant relationship was found between age and knowledge level ($P = 0.000$).

Table (1). Participants' knowledge of breast cancer risk factors. (N= 430)

Characteristics	Frequency	Percent
Wearing tight-fitting bras for extended periods.	230	53.5
Older age	142	33.0
Nulliparity	131	30.5
Late menopause	162	37.7
Early menarche	93	21.6
Late pregnancy of first child	81	18.8
Obesity after menopause	124	28.8
Taking OCP	266	61.9
Unhealthy habits (smoking, drinking, etc)	253	58.8
Breast imaging	236	54.9
Large breast	104	24.2
Regular daily exercise	177	36.5
Family history	256	59.5
Breastfeeding	285	66.3
Unhealthy diet	266	61.9
Sleep disorders	157	36.5

2) Breast cancer signs and symptoms:

The mean score for the "Signs and Symptoms" section was 3.38 (± 1.67), indicating a generally good level of knowledge among participants, distributed as weak (19.1%), moderate (7.7%), and excellent (73.3%).

The most recognized signs and symptoms were a suspicious mass (79.5%), breast swelling and abnormal discharge (71.9%), and skin changes (70.9%). However, only 65.1% identified nipple distortion, and 50.2% recognized itching and skin lesions around the breast. (Table 3)

No significant associations were found between knowledge of (BC) signs and symptoms and participants' age ($p = 0.638$), marital status ($p = 0.422$), family history ($p = 0.252$), or personal history of (BC) ($p = 0.189$). However, a significant relationship was found between education level and knowledge of signs and symptoms ($p = 0.035$).

Table (3). Participants' knowledge of breast cancer symptoms and signs. (N= 430)

Characteristics	Frequency	Percent
Breast lump	342	79.5
Breast swelling and discharge	309	71.9
Changing the skin form	305	70.9
Nipple distortion	280	65.1
Itching and Skin Lesions Around the Breast	216	50.2

3) Breast cancer screening knowledge:

Breast cancer screening knowledge varied among participants, with 53.0% showing low knowledge, 38.1% moderate, and only 7.7% high. Most participants (80.7%) correctly identified (BC) as the most common cancer among women worldwide, and 78.6% believed it is curable. However, only 47% knew the ideal timing for (BSE). The recommended age to start BSE (21.2%) and mammography (40.9%), and their recommended frequency (39.8% for BSE and 42.1% for mammograms), was lower. (Table 4)

While 38.8% knew mammograms were the preferred screening method, only 33.7% were aware of its safety, and 54.2% knew a prior doctor's examination was needed. The internet (27.9%) and television (21.6%) were the most common sources of information, but 57.9% had no formal training on BSE. Only 19.3% received instruction from a doctor, and 16.3% from online sources. Significant associations were found between knowledge levels and age ($p = 0.000$), marital status ($p = 0.019$), and family history of (BC) ($p = 0.004$). However, no significant correlations were observed with education ($p = 0.470$) or personal history of (BC) ($p = 0.423$).

Table (4). Participants' knowledge of breast cancer screening. (N= 430)

Characteristics	Frequency	Percent
Breast cancer is the most common cancer among women worldwide	347	80.7
Breast cancer is curable	338	78.6
Regular BSE improves patient outcomes	337	78.4
BSE helps in early detection of the disease	346	80.5
Training on BSE	83	19.3
Age of starting BSE	91	21.2
The best time for BSE before menopause	204	47.4
The best time for BSE after menopause	205	47.7
Frequency of BSE	171	39.8
The Mammogram is the best method for screening	167	38.8
Safety of mammogram	145	33.7
Pain and discomfort after mammogram	102	23.7
Doctor examination before the mammogram	233	54.2
Age of starting mammogram	176	40.9
Frequency of mammogram	181	42.1

Attitudes towards Breast cancer screening:

The mean score for teachers' attitudes toward (BC) screening was 7.10 (± 2.71). A positive attitude was exhibited by 65.1% of participants, 18.4% had a neutral stance, and 15.1% displayed a negative attitude. Most participants (82.3%) believed that (BSE) aids in early detection of BC, and 81.9% agreed that early detection improves prognosis. Interestingly, 76.0% considered BSE important even without risk factors, and similar percentages for obesity (72.3%), family history (76.5%), stress (69.8%), and lack of exercise (68.6%). However, only 43.3% were willing to participate in awareness campaigns. (Table 5)

Significant associations were found between attitudes and both age ($p = 0.001$) and educational level ($p = 0.003$). No significant correlations were observed with marital status ($p = 0.466$), family history ($p = 0.744$), or personal history of BC ($p = 0.880$).

Table (5). Participants' attitude toward breast cancer screening. (N= 430)

Characteristics	Frequency	Percent
BSE is helpful in early detection of breast cancer	354	82.3
Early detection improves prognosis	352	81.9
No need for BSE if I don't smoke or drink	327	76.0
No need for BSE if I'm not obese and on a healthy diet	311	72.3
No need for BSE if there is no family history	329	76.5
No need for BSE if there are no stress or sleep disorders	300	69.8
No need for BSE if I don't take OCP	295	68.6
No need for BSE if there is no radiation exposure	292	67.9
No need for BSE if I do regular exercise	295	68.6
Willing to participate in awareness campaigns	186	43.3

Breast cancer screening Practice:

Frequent (BC) screening was reported by 65.1%, while 38.8% practiced it rarely, and 7.7% did not screen at all. Only 8.4% performed monthly BSE, with 45.1% not knowing how to perform BSE. Annual mammograms were done by 16.0%, while 58.6% never had one, with 30% unaware of the procedure. Reasons for avoiding mammograms included shyness (21.4%), fear (18.6%), and cost (2.8%). Most participants (77.2%) would visit a doctor upon noticing symptoms, (Table 2). Significant relationships were found between breast cancer screening practices and educational level ($p = 0.025$), marital status ($p = 0.041$), and family history ($p = 0.009$). However, no associations were observed with age ($p = 0.095$) or personal history of breast cancer ($p = 0.890$).

Table (3). Participants' practice toward breast cancer screening. (N= 430)

Practice	Frequency	Percent
No Practice	33	7.7
Rare	167	38.8
Occasional	140	32.6
Frequent	280	65.1
Consistent	33	7.7

DISCUSSION

Several studies have been conducted in western and eastern Libya to assess the knowledge, attitudes, and practices regarding breast cancer (BC). This study is the first to shed light on breast cancer awareness among Libyan female teachers in Misurata city.

Our findings show that 60.5% of participants exhibited a low level of knowledge about BC risk factors, while 73.3% demonstrated excellent knowledge of BC signs and symptoms. In terms of screening, (53%) had insufficient knowledge, though 65% displayed a positive attitude, and 65.1% reported frequently practicing BC screening.

Breast cancer risk factors can be categorized as modifiable and non-modifiable. Non-modifiable factors include sex, age, family history, genetic mutations, and previous breast conditions (Łukasiewicz et al., 2021). In our study, approximately 60% of participants were knowledgeable about non-modifiable risks like family history, breastfeeding, and breast imaging but showed low

awareness of advanced age (33%), late menopause (37.7%), early menarche (21.6%), and large breast size (24.2%). This is consistent with other studies in Libya, such as in Benghazi, where 88.5% of women recognized breastfeeding's protective role, but only 34% in Tripoli did (Taher et al., 2016; Ziyo et al., 2018). Awareness of age as a risk factor was low across the country, with similar findings in Derna (38%) (Elzahaf et al., 2018), and Misurata (33%). (El-Hamadi et al., 2019) reported better awareness of (BC) risk factors (52.7%). In our study, only 37.7% recognized late menopause as a risk factor, and early menarche (before age 12) had the lowest awareness at 21.6%. These results align with previous studies showing similar or lower awareness across Libya (El-Hamadi et al., 2019; Elsaid & Tunis Meidan, 2023; Elzahaf et al., 2018).

In other Arab countries, knowledge of family history as a BC risk was relatively high, with 75.4% in Jordan (Al-Mousa et al., 2020), and 59.1% in Saudi Arabia (Almanie et al., 2018). But, awareness of age as a risk factor remained low (Abbas & Baig, 2023; Al-Mousa et al., 2020; Almanie et al., 2018). In Jordan, 56.1% and (67.6%) were aware of radiation exposure and not breastfeeding as risks (Al-Mousa et al., 2020), while in Iran, 87% of women and 68% In Qatar knew nulliparity increased BC risk (Atashi et al., 2020; Hamed et al., 2022).

Modifiable risk factors for BC include the use of oral contraceptives, alcohol consumption, smoking, unhealthy diets, and lack of regular exercise (Łukasiewicz et al., 2021). In the current study, 61.9% of participants recognized oral contraceptive use and unhealthy habits, consistent with findings from Tripoli (63.4%) and other Libyan studies (Elzahaf et al., 2018; Taher et al., 2016). While 61.9% of Misurata teachers were aware of the impact of an unhealthy diet, lower awareness was reported in Tripoli (45.2%), Benghazi (45.7%), and Derna (40%) (El-Hamadi et al., 2019; Elzahaf et al., 2018; Ziyo et al., 2018). Only 36.5% of our participants knew regular exercise reduces BC risk, a much lower figure than Ziyo *et al.*'s study (65.2%) (Ziyo et al., 2018).

Approximately 54% of participants believed wearing tight-fitting bras for long periods was a BC risk, higher than the 15.1% reported in Jordan (Al-Mousa et al., 2020). Awareness of high glycemic index foods and low-fiber diets as BC risk factors was poor, with 31.2% recognizing these as risks, similar to figures from other surveys (Abbas & Baig, 2023; Al-Mousa et al., 2020). By contrast, 91.9% of Iranian women knew regular exercise could protect against BC (Atashi et al., 2020). Sleep disorders as a risk factor were poorly recognized by 36.5% of participants, in line with findings from the UAE 13.8% (Abbas and Baig, 2023). A significant relationship between participants' age and knowledge of BC risk factors was found, consistent with (El-Hamadi et al., 2019) findings that education and marital status also influenced knowledge and attitudes. However, Elzahaf *et al.* (2018) found no significant demographic associations. The overall low awareness of modifiable risk factors highlights the need for targeted education to promote BC prevention and screening.

Awareness of BC warning signs can lead to earlier detection and better treatment outcomes. In this study, 73.3% of participants had excellent knowledge of BC symptoms, similar to findings from Tripoli (El-Hamadi et al., 2019). The most recognized symptom was a breast lump 79.5%, which aligns with the Tripoli study (El-Hamadi et al., 2019), though higher knowledge levels were reported in other Libyan cities (Elsaid et al., 2023; Elzahaf et al., 2018). About 71% of participants identified breast swelling, discharge, and skin changes as warning signs, which is lower than in eastern Libya, where over 90% of participants recognized these symptoms (Elzahaf et al., 2018). Knowledge of nipple distortion and skin lesions around the breast was consistent with previous Libyan studies (El-Hamadi et al., 2019; Elsaid & Tunis Meidan, 2023; Elzahaf et al., 2018), but Iranian midwives showed superior knowledge (95%) which might be due to their health-related education (Atashi et al., 2020).

Higher education was associated with better knowledge of BC signs, unlike in Iran, where family history rather than education correlated with knowledge (Atashi et al., 2020). Screening knowledge was varied: 53% had low awareness, and only 7.7% showed good knowledge. Other Libyan studies reported higher levels of screening awareness (Ziuo et al., 2018; Elzahaf et al., 2018), though Misurata participants demonstrated better knowledge compared to respondents from Qatar and Bahrain (Donnelly et al., 2015; Fikree et al., 2011). Knowledge of BC as the most common cancer among women was high (80.7%), in line with other studies (Alwan et al., 2012; Elsaid & Tunis Meidan, 2023), and over 70% recognized its curability if detected early, similar to Jordan (Al-Mousa et al., 2020) and the UAE (96.6%) (Abbas and Baig, 2023).

Regarding breast self-examination (BSE), 80% of participants knew it aids in early detection, which aligns with studies from Benghazi and other Arab countries (Al-Mousa et al., 2020; Eldessouki et al., 2019; Ziuo et al., 2018). However, only 19.3% of participants had been trained to perform BSE, with higher training rates reported in Tripoli (62%) and lower rates in India and Iran (3.1%) (Atashi et al., 2020; Prusty et al., 2020). Less than one-fifth of participants knew the correct age to start BSE, similar to other studies in Libya (Ziuo et al., 2018) and all over the world (Akpınar et al., 2011). The best time to perform BSE was known by 47.4%, slightly lower than Turkish women (55.6%) (Akpınar et al., 2011). Knowledge of the correct frequency of BSE was low, consistent with findings from eastern Libya (Ziuo et al., 2018) and Egypt (Eldessouki et al., 2019).

Mammogram awareness was insufficient, with only 38.8% recognizing its importance, which is lower than 80% of UAE residents (Abbas and Baig, 2023) and Jordanian women (Al-Mousa et al., 2020). Safety concerns about mammograms persisted, with only 33.7% of participants recognizing them as safe. In Tripoli, 60% believed mammograms could cause BC (Taher et al., 2016), and, like other studies, mammogram frequency knowledge was insufficient (Abbas and Baig, 2023). Respondents' main sources of BC information were the internet (28%), television (21.6%), and healthcare professionals (19%), similar to findings from Ethiopia (Asmare et al., 2022) and Iraq (Alwan et al., 2012).

A positive attitude toward BC screening was shown by 65.1% of participants. While 15.1% showed a negative attitude, aligning with other studies from Libya (Ziuo et al., 2018) and other African Arab countries (Eldessouki et al., 2019). Attitudes toward screening were significantly associated with age and education, similar to other surveys (Abbas & Baig, 2023; Elzahaf et al., 2018). However, an Iranian study found family history and marital status significantly influenced screening attitudes (Atashi et al., 2020), while another Libyan study found no association between attitudes and demographic factors (Elzahaf et al., 2018). Contrary to previous studies in Libya and other countries where BC screening practice was low (Atashi et al., 2020; Ziuo et al., 2018), 65.1% of our participants frequently practiced screening, with only 7.7% never doing so. Screening practice was significantly associated with education, marital status, and family history, which is supported by other studies (Atashi et al., 2020; Ziuo et al., 2018). However, an Iranian study on midwives found no impact of marital status and family history on BC screening (Atashi et al., 2020), and a 2017 Libyan study showed no association between breast examination and demographic factors (Elzahaf et al., 2018).

This study is more comprehensive than previous Libyan surveys, as it extensively evaluated BC awareness, including risk factors, symptoms, screening methods, and the importance of early diagnosis. However, it was limited by its focus on female teachers and the use of convenience sampling, which may limit generalizability. Despite these constraints, the findings may prompt a reevaluation of the national health education strategy.

The lack of BC knowledge among educated Libyan women highlights the need for widespread dissemination of information about BC, its risk factors, and screening methods. While the effectiveness of BSE in reducing mortality is debated (Thomas et al., 2002), it remains a culturally appropriate and cost-effective method for resource-limited countries like Libya. Until routine mammography is available, promoting BSE should be prioritized. A comprehensive national policy is needed to raise awareness and improve women's health-seeking behaviors.

CONCLUSION

Women in Misurata city have a positive attitude toward (BC) screening. However, their poor knowledge will not help them to adopt proper practice techniques. Adoption of a dual approach integrating primary prevention measures to decrease the overall risk burden in the community with early detection methods to improve patient outcomes is advised. In addition, Further research is needed to identify the magnitude of the problem nationwide, assess responses to future corrective measures, and identify barriers and promoters of breast cancer screening.

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ETHICS

The data collection tools were anonymous, and data confidentiality was maintained throughout the study.

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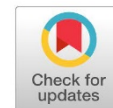
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Case Report

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Giant Vesical Calculus Presented with Anuria in a Young Male Patient: A Case Report

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Abstract

A giant Vesical calculus (GVC) is a calculus that weighs more than 100 grams (g) or measures more than 4 centimeters (cm) in its widest diameter. It is a rare clinical condition in adults. Over the past few years, the number of patients with GVCs has decreased due to the wider availability of healthcare and improved diagnostic modalities. In the literature, there are very few reports of GVCs leading to bilateral obstructive uropathy and anuria. Here, we present a case of azotemia and anuria in 39-year-old male Libyan man. His workup revealed a giant vesical calculus (10×9×6) centimeters, and an open Cystolithotomy was performed. A giant brown hard vesical solitary calculus weighing 435 grams was removed. He passed an uneventful post-operative course, apart from a short period of post-obstructive diuresis, and discharged home on the eighth postoperative day with almost normalized renal function.

Keywords: Giant vesical Calculus, Hydroureteronephrosis, Anuria, Young Male, Suprapubic Cystolithotomy, Benghazi, Libya

INTRODUCTION

Bladder stones are responsible for 5% of all urinary system stones and seen more frequently in men than women, and they rarely develop spontaneously (Ofloglu et al, 2013). Urinary tract infection, urethral stricture, benign prostatic hyperplasia, and intravesical foreign body encrustation are the most common causes of urinary bladder calculi formation (Faisal et al., (2022). Fewer than 100 cases have been reported in the literature with a weight more than 100 grams and almost all of them had bladder outlet obstructions (Elkhafifi et al., 2021). Vesical calculi are often of small to moderate size, but at times can attain a huge size.

They may be smooth or multifaceted. Struvite stones are usually smooth and are commonly responsible for giant GVCs, while the multifaceted stones are typically composed of calcium oxalate (Lawal et al., 2016). Vesical calculi have a varied presentation, ranging from completely asymptomatic to dysuria, lower abdominal pain, gross hematuria, and retention (Vidhyathy et al., 2020). However, it is rare for the stone to become so large as to compress both ureteric orifices and block the bladder outlet, causing renal failure (Mukherjee et al., 2020). Here, we present a case of a GVC presented with anuria and renal impairment; the patient was managed successfully with an open cystolithotomy.



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CASE Report

A 39-year-old male Libyan patient presented to the outpatient department with anuria for a duration of two days prior to his hospitalization. For the past seven months, he has complained of bilateral flank pain and dull Suprapubic pain and heaviness. The patient's medical history indicated that both obstructive and irritative symptoms had been observed for a duration exceeding 15 years. There was no history of hematuria, catheterization, trauma, or instrumentation. Due to the lack of medical facilities in such areas of the country, he claimed that he only received traditional therapy and unspecified antibiotics for the presumptive diagnosis of UTIs.

On general physical examination, the patient was afebrile, conscious, and oriented, had mild pallor (2+), and was mildly dehydrated. His vital signs were stable. Abdominal examination revealed local cautory marks, soft, lax upper abdomen, mild tenderness, and there is a hard mobile mass in the Suprapubic region that is deeply palpable. A digital rectal examination disclosed a prostate of normal size and consistency and an easily palpable stone. An attempt at urethral catheterization was unsuccessful due to the resistance encountered at the bladder neck by the stone. His baseline investigations were as follows: Hemoglobin, 8.7 g /dL; total leukocyte count, $9.1 \times 10^9/L$. In addition, serum creatinine is 8.7mg/dL, Urea 107mg/dL. His electrolytes were within normal limits. Routine urinalysis which was performed 3 to 4 days before presentation to our hospital showed a reddish-yellow aspect, turbid and an acidic PH, 1+ albuminuria, 1+ blood, while being negative for nitrates and bilirubin. Urine microscopy revealed 8-10 HPF leukocytes 20-25 HPF red blood cells, and neither cast nor crystals were present. Urine culture was negative.. The plain abdominal x-ray (KUB) showed a large radiopaque shadow in the pelvic region (Figure 1).



Figure (1). plain abdominal x-ray (KUB) showed a large vesical calculus occupying the pelvic region.

Abdominopelvic ultrasonography disclosed bilateral moderate Hydroureteronephrosis and a thickened bladder wall with a large stone about 6.7×5.9 cm with a normal sized prostate and echogenicity. On day 2, under spinal anesthesia, a urethroscopic evaluation was performed that showed a normal urethra, non-obstructed prostatic lobes, and a patent bladder neck. Cystoscopy could not be done due to the resistance encountered by the obstructed stone at the bladder neck level. Through a pfannestiel incision, he underwent an open cysto-lithotomy and a giant yellowish-brown calculus measuring 10×9 ×6 CM and weighing 435 grams was removed [Figure 2].

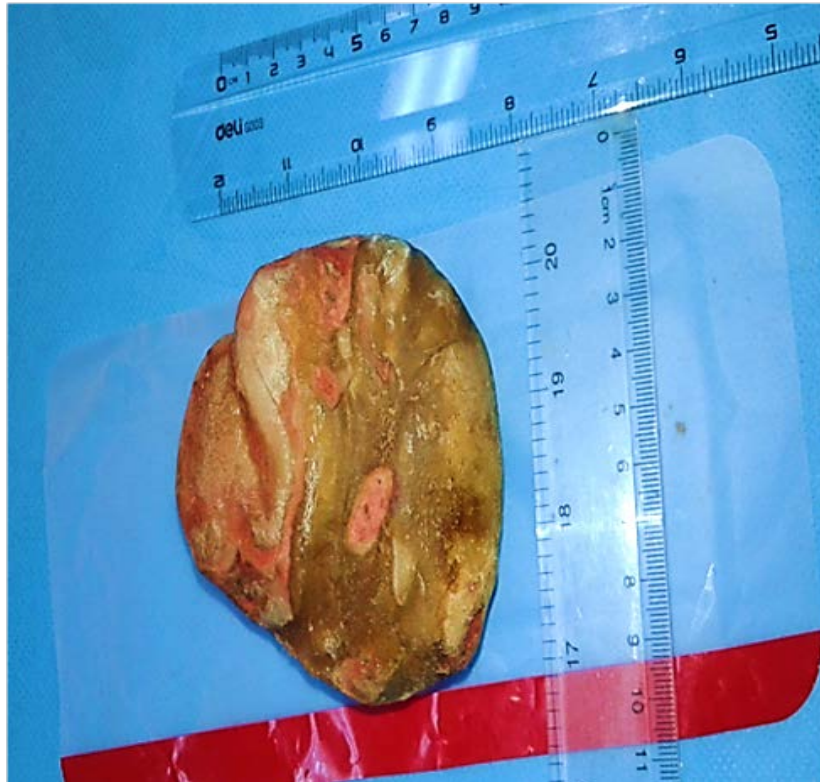


Figure (2). Giant vesical calculus extracted by cystolithotomy measuring 10x9x6 cm and weighing 435 gram.



Figure (3). Gross appearance of the calculus immediately post -cystolithotomy

The calculus was adherent to the bladder mucosa, which was acutely inflamed and edematous, but there was no visible lesion necessitating a biopsy. The urinary bladder and abdominal wall were closed accordingly over a 20 Fr three-way Foley catheter and fixation of the pelvic drain. He had an uneventful post-operative course, except for a short period of diuresis lasting for two to three days. On the second post-operative day, the pelvic drain was removed and he was discharged nine days later with almost normal renal functions (S. cr. creatinine 1.5 mg/dl). Unfortunately, our patient was from the countryside, and he lost scheduled follow-up and chemical stone analysis.

DISCUSSION

The term “giant vesical calculus” refers to any bladder stone weighing more than 100 g or measuring more than 4 cm in its largest diameter (Lawal et al., 2016)

- Bladder stones are commoner in men than in women with an incidence of 95% (Ismail et al., 2021). Most bladder stones are in the range of 1 to 2.5 cm and weigh less than 100gm. (Arthure, 1953). The biggest vesical calculus described weighed 6294 g (Diniz et al., 2017) & the mean size in the longest diameter was 8.38 cm, the bigger one had 17 cm in the longest diameter (Molla et al., 2022).
- Primary or endemic bladder stones are formed in the absence of underlying uropathy, which is less common in the developed world (XWei et al., 2022). With the development of medicine and the improvement of living standards, the incidence of bladder stones has progressively decreased (Bestari et al., 2022). Bladder stones can typically be classified as primary, secondary, or migratory based on the etiology. Spontaneous bladder stones rarely occur in adults; therefore, predisposing factors must be explored to identify the cause and prevent recurrence (Hamad et al., 2006).

The typical symptoms of bladder calculi are Suprapubic pain, dysuria, intermittency, terminal hematuria and urinary retention (Parma et al., 2018). Acute renal failure with features of oliguria and raised creatinine is a rare (Becher et al., 1978). It is more often seen in low socioeconomic and underdeveloped countries secondary to malnutrition and consists of predominantly ammonium urate and calcium oxalate stones. Bladder calculus is usually associated with renal or ureteric calculi and they rarely occur without upper tract stones as was seen in our index case (Otieno et al., 2015). As the majority of bladder calculi are radiopaque can be detected by plain radiograph (KUB) (G Shilpi et al., 2007). Other investigations, which can show bladder calculi, are ultrasound, CT scan, magnetic resonance imaging and intravenous urogram but non-contrast-enhanced CT is the investigation of choice as it has remarkable sensitivity in detecting urinary tract stones, including uric acid stones. It can reveal the concentric nature of stones (Mazlan et al., 2022).

The treatment of bladder stones depends on the size and the composition of the stone, the comorbidities of the patient, the presence of previous surgery, and anatomic abnormalities of the lower urinary tract, costs, as well as the equipment available. It is essential to eliminate the causative factors in order to ensure therapeutic success (Papatsoris et al., 2006). Open cystolithotomy is still the preferred type of surgery for bladder stones measuring more than 4 cm as proposed by Torrecelli and colleague (Torricelli et al., 2013). Though we are moving toward the era of minimally invasive procedures methods such as extracorporeal shock wave lithotripsy and transurethral cystolithotripsy still have their limitations. The prolonged surgery increases the risk of complications such as urethral stenosis, urethral trauma, and visual disturbance due

to hematuria and stone dust (Thakur et al., 2007). Patients with large obstructive bladder stones and renal impairment should be monitored for post obstructive diuresis in the early postoperative period. Recovery of renal function after stone removal depends on the extent of renal damage. All the authors of giant bladder stones with renal failure mentioned improvement in renal function after cystolithotomy. In some cases, the recovery in renal function was complete (Ofluoglu et al., 2013, LaiAY-H et al., 2007, Wei & Wang 2010, Aron et al., 2003); however, in others, either the recovery was partial or there was no record of renal function beyond the initial 3–5 days of surgery (Kamal et al., 2008, Komeya et al., 2013, Hassan et al., 2019). Minimal data exist on the causes, incidence and management of giant bladder stones considering their rare occurrence (Agrawal et al., 2019). During the last 20 years, only a handful of case reports reported the development of kidney failure due to bladder stone [Table 1].

Table (1). Showing Most of the Cases of GVC presented with Obstructive Uropathy and Renal Impairment during the last 20 years.

Author & year	Age	Sex	S. Cr on admission	Symptoms	Size	Weight	Treatment	S. Cr on discharge
Our case , 2024, <u>Libya</u>	39	♂	8.7mg/dl	Anuria and renal impairment	10×9×6 cm	435 gms	Cystolithotomy	1.5mg/dl
Molla <i>et al.</i> , 2023, <u>Ethiopia</u>	25	♂	4.29 mg/dl	Suprapubic pain, Dysuria, difficulty of Urination	10×6 cm	260 gms	Cystolithotomy ,Resecitation, catheterization	1.1 mg/dl
Bestari <i>et al.</i> , <u>Indonesia</u>	43	♂	9m/dl	Dysuria, intermittent urination, bilateral flank pain, gross hematuria recently	10×9×7 cm	Not mentioned	HD and cystolithotomy	6.6mg on second post-operative day
Mazlan <i>et al.</i> , 2022 <u>Malaysia</u>	30	♂	15.12 mg/dl	Intermittent hematuria and lower abdominal pain	15× 10×10 cm	1000 gms	PCN+HD+ cystolithotomy	Marked Improvement
Wei X <i>et al.</i> , 2022 <u>China</u>	31	♂	8.4 mg/dl	LUTs, Urine retention and Milky – white urine	11×11 cm	Not mentioned	Cystolithotomy	Not mentioned
Mukherjee <i>et al.</i> , 2021 <u>UK</u>	53	♂	2.9m/dl	Frequency, urgency, poor stream, S.p.pain	9×6.5×4.5 cm	Not mentioned	Cystolithotomy	Normalized
Agrawal <i>et al.</i> , 2019 <u>USA</u>	56	♀	6.1 mg	Lower abd. Pain, Dysuria ,Frequency	11×11×10.4cm	Not mentioned	PCN + Cystolithotomy	Not mentioned
Hassan <i>et al.</i> , 2019 <u>USA</u>	57	♀	6 mg /dl	Recurrent UTI , bilateral flank pain and sp.p.pain	11×9.5×8.6cm	1300 gms	PCN + Cystolithomy	2.6 mg/dl on second week
Parmar <i>et al.</i> , 2018 <u>India</u>	35	♂	5.4mg/dl	LUTS , N/V and oliguria	Not mentioned	490 gms	U. Cath. + cystolithotomy	1.4mg/dl
Diniz <i>et al.</i> , 2017 <u>Brazil</u>	52	♂	6.3 mg/dl	Acute renal failure	10.7×7.7×5.8cm	623 gms	Cystolithotomy	2mg/dl
Otieno <i>et al.</i> , 2015 <u>Kenya</u>	52	♂	2.844mg/dl	Dysuria , overflow incontinence, colicky lower abdominal pain & swelling and constipation	8×7×7 cm	260 gms	Cystolithotomy	Not mentioned

Author & year	Age	Sex	S. Cr on admission	Symptoms	Size	Weight	Treatment	S. Cr on discharge
Komeya et al., 2013 japan	81	♂	8.09 mg/dl	Renal failure	7× 6× 6 cm	Not mentioned	Urethral cath. + Cystolithotomy	2.53 mg/dl on Third post-Operative day
Ofluoglu et al., 2013 <u>Turkey</u>	56	♂	1.6mg/dl	Nocturia ,dysuria and mild sp.p pain	11×10×6.5 cm	402 gms	Cystolithomy	1.2 mg
Wei et al., 2010 <u>China</u>	31	♂	8.09 mg/dl	Repeated UTIs and lower abdominal pain	11 cm	Not mentioned	Cystolithotomy	Normalized after two weeks
Kamal et al., 2008 <u>Canada</u>	30	♂	8.60 mgs	Decrease urine stream and prolonged voiding time	Not mentioned	95 gms	Cystolithotomy	1.87 mgs
Lai et al., 2008 <u>Taiwan</u>	69	♂	7.59 m/dl	Repeated UTIs and lower abdominal pain	11×8×7 cm	320 gms	Cystolithotomy	1.40 mg/dl
Thakur et al., 2007 <u>India</u>	72	♂	9 mg/dl	Urine retention and sp.p. Pain	6.6×6.25 cm	305 gms	B/L PCN+ cystolithotomy	5 mg/dl

Abbreviations:

S.cr.	Serum creatinine
H.D.	Hemodialysis PCN: Percutaneous nephrostomy
U.	Cath. Urethral catheter
S.p.pain	Suprapubic pain
UTI	Urinary tract infection
GVC	Giant vesical calculus

CONCLUSION

GVCs are a rare clinical condition in contemporary practice. Furthermore, it is extremely rare for it to present with obstructive uropathy and renal impairment. It should be considered in the differential diagnosis of any patient present with lower urinary tract symptoms. This case is interesting because of the following two reasons. Our patient did not have an infra-vesical obstruction that predisposed him to GVC, and he is among the rare patients with GVC who presented with anuria and severe renal impairment. However, we suspected recurrent UTIs during childhood as a possible cause of the vesical calculus. To the best of our knowledge, this is the first reported case in our department.

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