مجلة السعيدة للعلوم الطبية

Al-Saeeda Journal of Medical Sciences

Volume 5, Issue 1

ISSN: 2710-4877 (Print)

ISSN: 2710-4885 (Online)

SJMS

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Al-Saeeda Journal of Medical Sciences

Al-Saeeda Journal of Medical Sciences (SJMS) [ISSN: 2710-4877(Print); 27104885 (Online)] is the main scientific journal in the Faculty of Medical Sciences at Al-Saeeda University. ***SJMS*** is a refereed scientific journal aimed to publish original research articles in the different medical sciences disciplines.

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Al-Saeeda University Faculty of Medical Sciences

Published by Faculty of Medical Sciences - Al-Saeeda University. Dhamar City - Yemen

Al-Saeeda Journal of Medical Sciences

مجلة السعيدة للعلوم الطبية

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Office of Publication

Scientific Research Center, Faculty of Medical Sciences - Al-Saeeda University. Dhamar City – Yemen.

Publisher

Al-Saeeda University**.** Dhamar City – Yemen
E-Mail: editorsjms@su-edu.net,
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Content:

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Article Info:

Article type:
Research Article
Received:
01 April 2023
Revised:
13 April 2023
Accepted:
25 April 2023

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Conflict of interest: Nil

Al-Saeeda Journal of Medical Sciences (SJMS)

ISSN: 2710-4877 (Print); ISSN: 27104885 (Online)

Available Online at: journal.su-edu.net/index.php/su-journal

A peer reviewed medical journal published by Faculty of Medical Sciences - Al-Saeeda University, Dhamar, Yemen

SJMS; Volume 5, Issue 1; May: 2023; Page No. 1-16

In Vitro Quality Evaluation of Three Different Br ands of B1, B6 and B12 Tablets Marketed in Two Different Thermal Zones in Yemen

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Article Info:

Article type:
Research Article

Received:
01 April 2023

Revised:
13 April 2023

Accepted:
25 April 2023

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Conflict of interest: Nil

To cite this article:
Ahmed G. Al–Akydy, Ahmed Al-Washali and Samir Alsenafy, In Vitro Quality Evaluation of Three Different Br ands of B1, B6 and B12 Tablets Marketed in Two Different Thermal Zones in Yemen. *SJMS*. (2023); 5(1):P. 1-16

Abstract:

In Yemen, since medications are often purchased without adequately referenced quality standards and are not routinely evaluated, continuous evaluation of marketed drug products remains essential to ensure that the required quality is maintained post- marketing, which lead to protect public health,, maintain physicians' trust and save time and cost. The current study aimed to compare the quality of three different brands of B1, B6 and B12 tablets that are commercially marketed at two thermally different zones in Yemen. The same patch of the three brands were collected from Dhamar and Al- Hodidah cities and named as brand A, brand B and brand C. The quality control testing were determined through weight variation, hardness, disintegration, dissolution and content uniformity tests. All brands have been evaluated for compliance with United State Pharmacopeia standards. Quality control tests showed that B1, B6 and B12 of all brands were complied with the United State Pharmacopeia limits, except for B1 from Al-Hodidah city, and B6 from Dhamar city did not comply in content uniformity tests with pharmacopeia limits with by ± 2%. The brand B and C were physically and chemically good compared to the original brand A. in-vitro CQ testing of drug products after their marketing should be applied as replacement to in vivo bioequivalence testing under certain circumstances to maintain their safety and effectiveness, and to improve accessibility to health care and save money and time.

Keywords: *B1, B6, B12, quality control, United State Pharmacopeia, Thermal Zone.*

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Introduction

The quality of a generic drug product is an important factor to support its commercial marketing, saving money, improving accessibility and delivery to healthcare, and promoting patient's adherence [1-4]. However, general people and healthcare providers, rarely question the quality of marketed generic drug products, which may result in suboptimal use of them [2 -5].

Quality control (QC) is a part of the Good manufacture practice (GMP), and it involves tests of friability, weight variation, disintegration, dissolution, and drug assay [6-8]. It ensures that the drug adheres to the details as per the description and data stated on the drug label [9-10]. Furthermore, QC testing also ensures the safety, and effectiveness of the drug, and checks its purities and impurities, that may lead to potential degradation and alteration of chemical and pharmacological properties of pharmaceutical products, which have a significant effect on drug product quality, safety and efficacy [8-11].

Drug stability means the ability of the pharmaceutical dosage form to maintain the physical, chemical, therapeutic properties during the time of storage and usage by the patient [12,13]. The minor objective of pharmaceutical product stability is to find out the quality assurance that the product will remain at a desirable level of fitness throughout its validity during its existence in the pharmacy or its treatment regimen [14,15]. Therefore, one of the primary reasons for stability testing is to create confidence in the patient who is suffering from a disease and avoid the decomposition of unstable products to yield toxic material or losing its activity which leads to death due to the failure of treatment [15-18]. The second reason is related to the drug manufacturer protecting his brand name which evidenced and proved that it remains with effectiveness. In another way, the stability studies are used by manufacturers during the development of drug formulation to select the suitable excipients, to distinguish the best storage conditions, to determine the claimed drug product shelf life, and finally to verify that the manufacturing method or drug formulation has no changes which can adversely influence the product stability [17-19].

On the other hand, to maintain the activity and integrity of the pharmaceutical products, they should be stored in appropriate conditions to protect their composition, which is sensitive and/or decomposed by environmental factors. High temperature accelerates oxidation, reduction and hydrolysis reaction which lead to drug degradation, acidic and alkaline pH influence the rate of decomposition of most drugs, and moisture can catalyze chemical reactions as oxidation, hydrolysis and reduction reactions and promotes microbial growth, and

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light affects drug stability through its energy or thermal effect which lead to oxidation [20-21].

The B1, B6, and B12 vitamin is a micronutrient that comprises three water-soluble vitamins, which form essential and closely interrelated functions [22-24]. Their main physiological regulation processes are the metabolism of carbohydrates, amino acids, and fatty acids, and the synthesis of proteins, cholesterol, neurotransmitters, S-adenosyl methionine, and nucleotide bases [25-27]. They also reduce atherosclerosis-associated secondary outcomes. Moreover, it is known that B1, B6, and B12 vitamin deficiency leads to anemia, digestive and skin problems, infections, peripheral neuropathy, and psychiatric disorders [25-27].

In some countries, quality restricted procedures are not implemented by non-governmental organizations (NGOs) which work during drug purchase [28]. For drug purchase, the registration in resource-limited countries is usually approved under a prerequisite of a stability test; however, the approval of a drug in such countries is registered based on a simple review of documentation [28-30]. Furthermore, the technical assessment of the drug quality monitoring is imitated. Even if the efforts of such drug quality monitoring are being made in developing countries, only simple pharmacopeia test methods for quality confirmation exist and the stability test for generic drug products will not be performed [28-30].

In Yemen, since drugs are often procured without the quality standards of sufficient references and the stability of products not routinely assessed, ongoing evaluation of marketed products, including B1, B6, and B12 vitamins, remains essential to ensure that the desired quality is maintained post-marketing, to protect public health, and to retain general people and healthcare workers confidence. Therefore, this study designed to evaluate quality of two different national brands of B1, B6 and B12 tablets, through in vitro QC testing as per the United States Pharmacopeia (USP) [31-33] and to compare their quality with a foreign product that commercially available on Yemeni pharmaceutical market of two thermally different zones.

Materials and Methods

Study setting

All the analytical tests for the current study were carried out in the QC laboratories of Global Pharma Company, Sana'a, Yemen, from April to August, 2022.

Materials

Chemical agents (B1, B6, and B12 tablets)

The search in literature Supreme Board of Drug and Medical Appliances and the market survey indicated that three different brands of B1, B6,

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and B12 tablets were commercially available in retail pharmacies inthe Yemeni pharmaceutical market at the study time. Before purchase, label information of the included brands of B1, B6, and B12 tablets was checked for manufacturing company, the strength of B1, B6, and B12 in tablet, batch number, date of manufacture and expiring dates. Subsequently, the three different commercial brands of B1, B6, and B12 tablets were randomly purchased from different private retail pharmacies in Dhamar and Al- Hodeida cities. Thereafter, the tablets were randomly coded with the letters A1, A2, B1, B2, and C1, C2, as outlined in Table 1.

Table 1: Label information of the included brands of B1, B6, and B12 tablets

Brand	Code	M. Company	Country of origin	Strength		Dosage Form	No. of Batch	*M. Date	*Ex. Date
Neurobion	A	Merck	Austria	B1	100mg	Sugar-coated	339021A	4/2021	3/2023
				B6	200mg				
				B12	200mcg				
Neuromax	B	Global Pharma	Yemen	B1	100mg	Film-coated	21346	6/2021	6/2023
				B6	200mg				
				B12	200mcg				
Three- B	C	Biopharma	Yemen	B1	100mg	Film-coated	379T	11/2021	4/2023
				B6	200mg				
				B12	200mcg				

*M. date: Manufacturing date *Ex. Date: Expiry date

Equipments

Table 2: Equipments

No.	Name of equipment	Company	Country of origin
1.	Hardness tester	Pharmatest	Germany
2.	Analytical balance	Mettler Toledo	Germany
3.	Disintegration tester	Pharmatest	Germany
4.	Dissolution tester	Pharmatest	Germany
5.	HPLC	Waters	USA

Study design

The current study was designed as in vitro comparative study, where the three brands of B1, B6, and B12 tablets that are commercially

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available in the Yemeni pharmaceutical market were subjected to the QC tests procedures.

Quality control tests and calculations

All brands were subjected to the QC tests, that included method assay tests, hardness, weight variation test, disintegration time, and dissolution tests, according to United States Pharmacopoeia (USP) [31-33].

1. Non-official test methods

Hardness test

The crushing strength of the tablet was measured using an automatic hardness tester (Pharmatest, Germany). At first 6 tablets were picked randomly from 20 tablets. Force has been applied with the screw thread and pressed until the tablets have been fractured [22, 34-38].

2. Official test methods

2.1. Weight variation test

Twenty tablets were randomly selected from each brand and individually weighed using an analytical balance (Mettler Toledo, Germany). The mean and standard deviation (SD) were calculated for the tablets [22, 34-38]. Then the percentage of weight variation was calculated by using the following formula:

$$\% \text{ weight variation} = \frac{\mathbf{w1 - w2}}{\mathbf{w2}} \times \mathbf{100}$$

Where, w1 = individual weight of the tablet, and w2 = average weight of tablets.

Table 3: Weight Variation Limit

IP/USP	Limit [tablet]
< 130mg	±10
130 - 324 mg	±7.5
> 324 mg	±5

The result be accepted for the product if not more than two tablets which under the test be deviate from the limit of average weight [22, 34-38].

2.2. Disintegration test

Six tablets were randomly selected from each brand and placed in the disintegration apparatus (Pharmatest, Germany), which is filled with 900 mL of distilled water as disintegration medium, and maintained at 37±1°C. The time taken to disintegrate the tablet and pass through the mesh was recorded and the mean of time taken was calculated [22, 34-38].

2.3. Dissolution test (only Pyridoxine and Thiamine):

Preparation of mobile Phase

Methanol 700: Buffer 300: Triethylamine 1. adjust with H_3PO4 to a pH of 4.3

Buffer: Dissolve 0.234 g of NaH_2PO4 and transfer 0.1 ml of H_3PO4 to 300 ml of water.

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Table. 4: Dissolution parameter

Dissolution parameter	
Medium	900 ml of 0.1M HCl.
apparatus	2
time	60 min.
speed	75 rpm

Preparation of the standard

Weigh accurately equivalent to 50 mg of Thiamine RS and equivalent to 50 mg of Pyridoxine RS into 100 ml V.F, dissolve and dilute to volume with 0.1 M HCL and mix well. Transfer 5 ml of this solution to 50 ml V.F dilute to volume with medium and mix. (0.05 mg/ml of Thiamine and 0.05 mg of Pyridoxine).

Preparation of sample solution

Use the direct filtrate solution (0.05556 mg/ml of Pyridoxine & 0.05556 mg of Thiamine).

HPLC conditions for Thiamine

Column	**C8, 25 cm hypersil**			**Wavelength**	**280**	**Flow rate**	**2**
						End Time	**4**
Limit	**NLT**	**75**	**%(Q)**				

HPLC conditions for Pyridoxine

Column	**C8, 25 cm hypersail**			**Wavelength**	**280**	**Flow rate**	**2**
limit	**NLT**	**75**	**%(Q)**			**End Time**	**5**

3. Assay methods

3.1. Method:- HPLC Reference:- Thiamine HCLPreparation of mobile Phase: -

(Methanol: Buffer: Triethylamine) (700: 300: 1). adjust with H3PO4 to a pH of 4.3 Buffer: Dissolve 0.234 g of NaH2PO4 and transfer 0.1 ml of H3PO4 to 300 ml of water.

Preparation of the standard

Weigh accurately equivalent to 50 mg of Pyridoxine RS and equivalent to 50 mg of Thiamine RS into 100 ml V.F, dissolve and dilute to volume with 0.1 M HCL and mix well. Transfer 5 ml of this solution to 50 ml V.F dilute to volume with medium and mix. (0.05 mg/ml of Pyridoxine & 0.05 mg of Thiamine).

Preparation of sample solution

Use the direct filterate solution (0.05556 mg/ml of Pyridoxine &0.05556 mg of Thiamine).

HPLC conditions

Column-	**C18,15 cm hypersail**			**Wavelength**	**280**	**Flow rate**	**2**
limit	**NLT**	**90% to**	**120**			**End Time**	**4**

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3.2. Method :- HPLC Reference :- Pyridoxine HCLPreparation of mobile Phase: -

(Methanol: Buffer: Triethylamine) (700:300:1). Adjust with H3PO4 to a pH of 4.3 Buffer: Dissolve 0.234 g of NaH2PO4 and transfer 0.1 ml of H3PO4 to 300 ml of water.

Preparation of the standard:

Weigh accurately equivalent to 50 mg of Pyridoxine RS and equivalent to 50 mg of Thiamine RS into 100 ml V.F, dissolve and dilute to volume withmobile phase and mix well.

Preparation of sample solution

Grind not less than 10 tablets and weight equivalent to one tablet into100 ml V.F dissolves with mobile phase and sonicates for ten minutes, thenlet cool and complete to volume with the mobile phase.

HPLC conditions

Column:-	**C8, 25 cm hyper sail**			**Wavelength**	**280**	**Flow rate**	**2**
limit	**NLT**	**75**	**%(Q)**			**End Time**	**5**

3.3. Method :- HPLC Reference :- Cyanocobalamin Preparation of mobile Phase: -

Methanol and water (7:13)

Preparation of the standard:-

5 µg/mL of cyanocobalamin from USP Cyanocobalamin RS in water.

Preparation of sample solution: -

Finely powder NLT 20 Tablets. Transfer a portion of the powder, equivalentto 500 µg of cyanocobalamin, to a100-mL volumetric flask, add 60 mL of water, and sonicate for 5 min. Dilute with water to volume, and filter.

HPLC conditions:-

Column:-	**C18, 15 cm hyper sail**	**Wavelength**	**361**	**Flow rate**	**2**
Limit	**NLT 90% to 120%**			**End Time**	**8**

3.4. Content uniformity test

The active ingredient uniformity test of the tablets was carried out using HPLC (Waters, USA). Active ingredient chemical identification and content uniformity tests were carried out according to the USP [31-33].

Data analysis

Weight uniformity, weight variation, hardness, dissolution, and disintegration times of B1, B6, and B12 tablets of each brand were analyzed by calculating the mean ± standard deviation (SD) for each parameter using the Excel program for Windows.

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Ethical consideration

This study was carried out after approval of ethical committee, faculty of medical sciences, Al-Saeeda University. Although the study did not involve human or animal subjects, informed consent was obtained before the collection of specimens.

Results and Discussion

Ongoing evaluation of the quality of generic drug products remains crucial to protect public health,, improve the confidence of clinicians and public and save money. QC involves specific instruments to ensure the quality of drug testing as per set guidelines [2 -5]. We assessed the pharmaceutical quality of an original brand and tow generic brands of thiamine, pyridoxine, and cobalamin tablet, that were commercially available on the Yemeni pharmaceutical market at the period of this study. All brands passed *in-vitro* quality testing like weight variation, drug assay, friability, disintegration, and dissolution tests, according to USP [31-33].

1. Non-official test results

Hardness test

Tables.5: Hardness test results for different brands of B1, B6 and B12 tablets

Hardness kg/cm^2 (Mean ± SD)				
	City			
Brand	**Dhamar**	**Al-Hodidah**	**Limit**	**Conclusion**
A	11.41±1.175	9.98±2.74	5-10 kg/cm^2	Unconformity
B	14.5±5.74	15.96±6.1		
C	9.1±1.06	8.21±0.94		Conformity

If the tablet is too hard, it may disintegrate in the required period and if it is too soft, it will not with stand the handling during subsequent processing such as coating or packaging and shipping operations[22, 34-38].Hardness was monitored using an automatic tablet hardness tester and the results were tabulated Table 5. Hardness range specification is 5 to 10 kg [31-33]. Therefore, the generic brand C was within the USP quality specification, where it passed the hardness test and was within the acceptable range in Dhamar and Al-Hodidah cities. However, the generic brands A and B in Dhamar and Al-Hodidah cities not fulfill the USP quality specification of

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hardness test by the average value that were not within the acceptable range. These findings are not similar to those of previous studies conducted in Albania [22].

2. Official tests results

2.1. Weight Variation test

Tables. 6: Weight Variation test results for different brands of B1, B6and B12 tablets from Dhamar City

Weight of Tablet (mg)				Deviation in weight From average (%)			Conclusion
N0.	**A1**	**B1**	**C1**	**A1 %**	**B1 %**	**C1 %**	
1.	744.6	634.6	598.7	6.6	1.2	-2.4	**Conformity**
2.	704.8	635.7	625.2	0.9	1.3	1.8	
3.	674.6	632.9	619.5	-3.3	0.9	0.9	
4.	665.1	615	599.4	-4.7	-1.9	-2.3	
5.	691.4	618.6	607	-0.9	-1.3	-1.07	
6.	696.1	625.9	625.2	-0.3	-0.1	1.8	
7.	647.2	625.9	617.4	-7.2	-0.1	0.6	
8.	683.3	590	612.5	-2.1	-5	-0.1	
9.	683.2	635.2	608.3	-2.1	1.3	-0.8	
10.	708.1	630.9	622.5	1.4	0.6	1.4	
11.	713.4	648.3	621.8	2.1	3.3	1.3	
12.	684.3	616.5	616.3	-1.9	-1.6	0.4	
13.	703.3	619.8	617	0.7	-1.1	0.5	
14.	721.3	622.3	602.7	3.3	-0.7	-1.7	
15.	728.3	620.8	620.4	4.3	-0.9	1.1	
16.	683	632.4	612.1	-2.1	0.8	-0.2	
17.	719.5	636.2	613.2	3	1.4	-0.06	
18.	711.6	636.3	611.3	1.9	1.4	-0.3	
19.	706.2	627.2	607	1.1	0.03	-1.07	
20.	693.8	636.4	616.2	-0.6	1.4	0.4	
Average Wight (mg)	698.1	627	613.6				
Limit	**More than 324**			**±5%**			

The results showed that the tablets were in limit of weight variation test which is not more than two tablets deviate from the average ≥ 5 [31-33].

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Tables. 7: Weight Variation test results for different brands of B1, B6 andB12 tablets from Al-Hodidah City

	Weight of Tablet (mg)			Deviation in weight From average (%)			Conclusion
N0.	**A2**	**B2**	**C2**	**A2 %**	**B2 %**	**C2 %**	
1.	718.7	635.5	628.9	1.2	1.03	2.5	
2.	719.4	644.1	614.8	1.3	2.4	0.2	
3.	689.6	627.7	615.4	-2.8	-0.2	0.3	
4.	678.6	624	619.4	-4.3	-0.7	0.9	
5.	705.5	614.1	604.7	-0.5	-2.3	-1.4	
6.	693.5	632.8	602.2	-2.2	0.6	-1.8	
7.	705.5	647.7	604.9	-0.5	2.9	-1.4	
8.	700.7	589.5	602.4	-1.2	-6.2	-1.8	**Conformity**
9.	731.5	627	621.4	3.1	-0.3	1.2	
10.	669.5	605.7	609.4	-5.6	-3.7	-0.6	
11.	710.8	618.7	617.3	0.1	-1.6	0.6	
12.	709.7	622.7	616.4	0.01	-1	0.4	
13.	714.6	634.5	613.5	0.7	0.8	0.008	
14.	739.5	633.4	619.5	4.2	0.6	0.9	
15.	733.2	628.3	610.7	3.3	-0.1	-0.4	
16.	735.2	616.9	601.8	3.6	-1.9	-1.9	
17.	746	646.6	614.7	5.1	2.7	0.1	
18.	699	641.4	609.3	-1.4	1.9	-0.6	
19.	705.7	643.2	616.4	-0.5	2.2	0.4	
20.	686.9	646.2	626	-3.1	2.7	2	
Average Wight (mg)	709.6	629	613.5				
Limit	**More than 324**			**±5%**			

The results showed that the tablets were in limit of weight variation test which is not more than two tablets deviate from the average ≥5%. Although the uniformity of weight does serve as a pointer to GMP, and the amount of the active pharmaceutical ingredients, especially for reproducibility of the product which is very essential for mass production ofany product [31-33]. Tables 6 and Table 7. show the average weight and weight variation of the different brands of tested B1, B6 and B12 tablets. Where, all brands A, B, and C in Dhamar and Al-Hodidah Cities conform to USP standards [31-33]. Therefore, all brands were within the USP quality specification. These results are consistent with those of previous studies carried out in Albania [22]

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2.2. Disintegration test

Tables. 8: Disintegration test results for different brands of B1, B6 andB12 Vitamin tablets

		Disintegration (min)				
	City		Differences Time (min)	Dosage form	Limit	Conclusion
Brand	Dhamar	Al-Hodidah				
A	30:32	32:35	2.3	Sugar coated	<60 min	Conformity
B	10:30	15:30	5	Film coated	<30 min	
C	10:03	9	1.03	Film coated	<30 min	

Disintegration test plays an important role in a tablet's dissolution. Therefore, the type, concentration, and efficiency of disintegrating to a large extent affected the dissolution [22, 34-38]. As per USP standards, the disintegration time limit for coated tablets is 30 minutes for film coated tablets and 60 minutes for sugar coated tablets. As per the QC tests performed in this study, the disintegration time in Dhamar City for brand A1 was 30.23 minutes, while it was 10.30 and 10.03 minutes for brand B1 and C1 respectively. On the other hand, the disintegration time in Al-Hodidah city for brand A2 was 32.35 minutes, while it was 15:30 and 9 minutes for brand B2 and C2 respectively, as shown in Table 8. Subsequently, the disintegration times of all brands A, B and C were under the USP limit [31-33], therefore, all brands in the current study conform to the disintegration test In addition, although the brand C had the faster disintegration time compared to brands A and B, all brands were within the USP quality specification [31-33]. These findings are in the line to those of previous studies conducted in Albania [22].

The disintegration time provides an idea of when the tablet will disintegrate and reach dissolution. The tablet disintegration time of brand C is less as compared to brand B, this can be attributed to that the powder blend of tablet C could have less binder excipient or there could be less force during tablet compression [22, 34-38].

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2.3. Dissolution test

Tables.9: Dissolution test results for different brands of B1, B6 and B12 tablets

		Dissolution (%)			
		City		Differences ratio	Conclusion
Brand	Vitamin	Dhamar	Al-Hodidah	%	
A	B1	96.9±0.72	94±0.56	2.9%	Conformity
	B6	117.5±2.03	115.6±1.13	1.9%	
	B12	-	-		
B	B1	90.5±0.66	88.9±027	1.6%	
	B6	117.9±4.57	120.1±0.43	2.2%	
	B12	-	-		
C	B1	88.1±0.99	87.6±0.69	0.5%	
	B6	117.8±2.61	117±1.33	0.8%	
	B12	-	-		
Limited		Not less than 75%			

The bioavailability and therapeutic effectiveness of oral conventional tablets of the drug depend completely on the dissolution rate of the drug. Therefore, it is very important to estimate the dissolution rate and compare the dissolution profiles of different marketed drug products. Dissolution test measures the extent of solution formation. In the current study, the rate of drug release was confirmed by the dissolution tests of brands of B1, B6 and B12 tablets. It was found that more than 80% of film and sugar coated tablets of all brands that collected from Dhamar and Al-Hodidah cities released within 30 and 60 minutes respectively, as outlined in Table 9. This means all brands meet USP quality specification [31-33] and was satisfactory from the dissolution point of view. Furthermore, this findings are in the line to those of previous studies that conducted in Albania [22].

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2.4. Content uniformity test

Tables 10: Content uniformity test for different brandsof B1, B6 and B12 tablets.

		Content uniformity %			
		City		Differences ratio	Conclusion
Brand	Vitamin	Dhamar	Al-Hodidah	%	
A	B1	92.64	97.28	4.64%	Conformity
	B6	111.36	105.47	5.89%	
	B12	105.4	97.6	7.8%	
B	B1	106.78	90.1	16.68%	
	B6	114.65	103.99	10.66%	
	B12	101.20	96.1	5.1%	
C	B1	110.85	88.32	22.53%	Unconformity
	B6	122.81	96.07	26.74%	
	B12	108.50	95.5	13%	
Limit		Not less than 90-120%			

The brands A and B of the B1, B6 and B12 tablets, which marketed in both Dhamar and Al-Hodidah city, complied to USP limits [22-33]. These results indicate a uniform distribution and an excellent quantity, as shown in Table6. However, thiamine of brand C, that marketed in Al- Hodidah city, and pyridoxine of brand C, that marketed in Dhamar city, did not comply with USP limits [31-33]. This can be attributed to a weak mixing process. These findings are not similar to those of previous studies carried out in Albania [22].

Conclusion

It can be concluded that thiamine, pyridoxine, and cobalamin tablets in all brands that marketed in two different thermal regions of Yemen during period of this study were within the USP limits regarding all QC-related tests, except thiamine and pyridoxine of brand C, that respectively collected from Dhamar city, and Al-Hodidah cities, did not comply with USP limits in content uniformity test. Therefore, in-vitro CQ testing of drug products after their marketing should be applied as replacement to in vivo bioequivalence testing under certain

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circumstances, and it must be performed from time to time in order to ensure that the quality of generic drug products within pharmacopeia standards and to maintain their safety and effectiveness, that lead to improve accessibility to health care and save money and time.

Acknowledgement

Authors thank Al-Saeeda University and pertinent staff for their support and cooperation. Authors also convey their sincere thanks to all students of the year of excellence in Pharmacy Department, Faculty of Medical Sciences – Al- Saeeda University (Almeqdad Ahmed Al-Naqeeb, Abdul-Jabbar Ahmed Al-Naqeeb, Abdul-Razzaq Hassan Al-Yari, Adnan Ibrahim Al-Sayad, Bassam Abdulatef Al-Mogahed, Diaa Lotf Al-Khawlani, Ezzaddin Ali Al-Hushaishi, Farhan Abdullah Al-Tubshi, Kamal abdh Al-Shakhdha, Mohammed Abdulrahman Al-Mawsheki, Mohammed Ahmad Al-Gidhei, Mohammed Ahmad Al-Shataif, Mohammed Ayash Al-Abrat, Mohammed Mugeb Swal, Waseem Mansour Al-Jaradi), for their help in successful completion of the study. Authors also convey their sincere thanks to the QC laboratories of Global Pharma Company, Sana'a, that accepted to perform QC tests and the use HLPC instrument for assay methods that are used in this study.

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Assessment of the Knowledge, Attitude, and Practice regarding Medication use in Pregnant Women at the University of Medical Center in Mukalla Directorate– Yemen.

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Article Info :

Article type:
Research Article
Received:
04 February 2023
Revised:
13 March 2023
Accepted:
22 March 2023

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Conflict of interest: Nil

Al-Saeeda Journal of Medical Sciences (SJMS)

ISSN: 2710-4877 (Print); ISSN: 27104885 (Online)

Available Online at: journal.su-edu.net/index.php/su-journal

A peer reviewed medical journal published by Faculty of Medical Sciences - Al-Saeeda University, Dhamar, Yemen

SJMS; Volume 5, Issue 1; May: 2023; Page No. 17-25

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Article Info:

Article type:
Research Article

Received:
04 February 2023

Revised:
13 March 2023

Accepted:
22 March 2023

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Conflict of interest: Nil

To cite this article:

Muna OS Alkatheri and Yahyakhamis Almualm, Assessment of the Knowledge, Attitude, and Practice regarding medication use in pregnant women at the University of Medical Center in Mukalla Directorate– Yemen. *SJMS*. (2023).; 5(1):P. 17-25.

Abstract:

Background: The possible teratogenic effects of various drugs and the mother's physiologic modifications and responses to pregnancy consider drug use during pregnancy a specific source of concern. Due to the risk to both the mother's health and the unborn child's life, drug use during pregnancy requires special consideration. The medication or metabolite concentration may even be higher in the embryo or fetus compartment than in the mother. The fetus is therefore treated as an "additional" patient and requires careful pharmacotherapeutic strategy. Lack of proper medication knowledge and practice among pregnant women might eventually have serious impacts on the health of both the mother and child. Thus, effective interventions are required to enhance pregnant women's knowledge, attitude, and practice regarding safe medication during pregnancy. Therefore, the purpose of this study was to assess knowledge, attitudes and practice (KAP) regarding medication use in pregnant women at the University Medical Center in Al-Mukalla District - Yemen. **Subject and Methods:** The study design was a descriptive cross-sectional -based study carried out from (September-November- 2023) among 400 randomly pregnant women attending clinics at the University of Medical Center. by using a self-administered questionnaire. **Results:** The statistical analysis for data obtained in this study showed that the majority percentage of the prevalence of drugs used during pregnancy was (52%), (49%) about half of pregnant women used drugs in the first trimester. Vitamins and antibiotics were the main drugs used (47%), (18 %) respectively. (3%) of pregnant women who had children with congenital malformation. They had a positive awareness of the medication risks on the fetus in pregnant women, the main source of information was doctors (84 %) but (2%), and (4%) of them they didn't know any things about the risk of the drugs on pregnant women or on the fetus and (4%) of them they had not any source of information, also we found that (45%) of the doctors didn't play a positive role to clarify the risk of the use of medicine to pregnant women to correct

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what we found in pregnant believes the highest percentage (59%) one was " Drink vitamins and drugs may increase fetus size and difficult delivery". Conclusion: The present study indicates that the prevalence of drugs used during pregnancy was mainly vitamins and antibiotics were used, On the other hand, the doctors didn't play a positive role to clarify the risk of the use of medicine by pregnant women or fetuses correctly. Although doctors and pharmacists were the main sources of information for pregnant women. Also, we found that the Drink vitamins and drugs may increase fetus size and difficult delivery" was the opinion of most pregnant women. It is therefore an urgent need to make them aware of the risks of drugs to ensure the safe use of medicines for pregnant women and fetuses.

Keywords: KAP, Medication use, pregnant women, Mukalla, Yemen

Introduction

Drug treatment during pregnancy presents a special concern due to the potential teratogenic effects of some drugs and physiologic adjustments in the mother in response to pregnancy. (1, 2). The use of drugs during pregnancy therefore calls for special attention because in addition to the mother, the health and life of her unborn child are also at risk. (2). The drug or metabolite concentration may be even higher in the embryonic or fetus compartment than in the mother. As a result, the fetus as an "additional" patient demands a strict pharmaco-therapeutic approach (3).

The choice of a medicine during pregnancy is even more difficult, since some medicines may have serious side effects on the fetus. The potential effects of medicine on the fetus should always be considered and the medication regimen during pregnancy should be chosen in such a way that it maximizes the effectiveness while minimizing the maternal and fetal risk (4).

Healthcare facilities should ensure that patients receive sufficient knowledge about their medications before leaving the facility. Counseling is one of the suitable methods to impart this required knowledge. Effective counseling has been associated with better and positive outcomes in terms of knowledge, attitude, and practice of the safe and effective utilization of medicines during pregnancy. Thus, enhancing medication safety during pregnancy (5).

Besides prescription medicines, pregnant women may also take OTC (over-the-counter) medicines which need to be identified and addressed accordingly (6). Both physicians and pharmacists have an important role in making pregnant women know about their conditions, any complications they have during pregnancy, and the medications they are taking. Studies reveal that pregnant women often take medicines without sufficient knowledge (6,7). Self-medication habits among pregnant women have been found to be common in many developing countries (7) and many of them might not know the reason for taking medication (8).

A patient's knowledge and capacity to get knowledge are important in the development of beliefs (8). Although some pregnant women may have sufficient knowledge about high-risk medication in pregnancy, there is a ''general fear'' from medications (9).
In Italy, previous studies showed that the prevalence of pregnant women using at least one medication was 48% after excluding vitamin and mineral products (10), 63.1% excluding supplements of iron and vitamins (9), and 70.4% excluding vitamins, mineral supplements, iron, and herbal or complementary medication products (10).
Therefore, the purpose of this study was to evaluate the knowledge, attitude, and practice (KAP) Practice regarding medication use in pregnant women at the University of Medical Center in Mukalla Directorate- Yemen.

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Material and Methods:

Study design: This was a descriptive cross-sectional study of the knowledge, attitudes, and Practice regarding medication use in pregnant women at the University of Medical Center in Mukalla Directorate– Yemen, from September to November - 2023.

Study area: This study will be carried out among pregnant women clinics at the University of Medical Center during the period (September- November 2023.

Sample size: Stratified random sampling is the method of selection sample, to ensure that all pregnant women at the clinic in the University of Medical Center during the period (September- November 2023) are included in the study sampling. The sample was randomly chosen 400 pregnant women who attend the clinical from the total number visitor pregnant women.

To do this research we need to know the sample size which is calculated by the following equation: - **$ss=Z^2 *(p)*(1-p)/c^2$**

Where:

ss=size of the sample

Z=confidence level when 95 = 1.96% as tabled.

P=expected proportion

C=margin of error at 5% (standard value of 0.05) -confidence interval.

SS= $(1.96)^2 * (1-840)/ (0.05)^2$

SS= 120 pregnant women.

So, we estimated a sample size of approximately for an assessment of the knowledge, attitude, and practice (KAP) Practice regarding medication use in pregnant women of 50%, a 95% confidence level, and a 5% margin of error.

Data collection: The data will be collected from different ages of pregnant women clinics in the University of Medical Center during the period (September- November) 2023. It was selected because provides childbirth services in the geographic area. The Directors of the Centers received a letter about the survey and explained the purpose and the methodology. A self-administrated questionnaire was designed, which included the following:

- The personal data (age, level of education, employment status, and marital status,)
- Medical data (self-assessed general state of health, medical history, gestational age, number of pregnancies)
- Awareness of the medication risks on the pregnant women and fetus.
- The main sources of knowledge information on medication use among pregnant women clinics at the University of Medical Center–Mukalla Directorate –Yemen
- The role of doctors in awareness of the medication risks to pregnant women
- Medication use beliefs about medications used among pregnant women
- Medication used among pregnant woman

Data analysis: The data will be coded and analyzed by statistical package for the social sciences (SPSS version 19) to ensure the accuracy of data such as frequencies and percentages were calculated and presented in tables and graphs by using computer office programs (word and excel office 2013)

Ethical Consideration: Approval of the project will be obtained from nursing college management and we took a letter to the University of Medical Center management to facilitate our work and data collection. So, participants will be informed about the research including the objectives and ensuring confidentiality those are agree to participate will be enrolled in the study, and that information will be taken in secrecy and will be used just for the research objective and for the benefit of the community.

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Results:

Four hundred respondents were approached for participation. All of them provided complete information. The demographic characteristics of the respondents were presented in **Table (1)** In our study, the majority percentage of the age was between (25-35) years (46 %,). But according to the level of education, Middle school was the higher percentage (36% and the majority percentage of Occupation was House-wife (80%). On the Other hand, Heath stated characteristics of the respondents were the majority percentage of the Number of pregnancies was (42 %) first pregnancy, We found in our study that the prevalence of medication used during the current pregnancy was 52%, and medications were commonly used in the second (38%) and third (37%) trimesters We found also that 6% of pregnant women had chronic disease and (3%) did not change the drugs of chronic disease after pregnancy. Also, we found 2% of our respondents had congenital malformation.

Figure (1) shows that the most common source of updated knowledge about drugs information regarding medication use in pregnant women at the University of Medical Center in Mukalla Directorate – Yemen was study (84%) from doctors and (20%) from pharmacists but (4%) of the participants reported that they hadn't any source of information about drugs.

In our study, we reported that the role of the doctor was to clarify the risk of medication used in pregnancy (52%), but (48%) nearly half of the doctors did not explain the risk to them, as shown in **Figure (4)**. On the other hand, the majority percentage of the awareness of medication risks on pregnant women and fetus were abortion (42%) on pregnant women and congenital malformation (64%) on the fetus but the pregnant women did not know any information of the risk of drugs on pregnancy (2%) or on the fetus (4%) that shows in **figure (5,6).**

Table (2) shows that the majority percentage of the pregnant beliefs about medications was that the doctors prescribed too many medicines (25%), The most medicines are additives (46%), natural remedies are safer than medicines(48%), and drink vitamins and drugs may increase fetus size and difficult delivery (59%).

Finally, from our study, we reported that the most common medications used were vitamins (47%), followed by antibiotics (18%) prescribed to pregnant women disorder (65%) among respondents. All drugs used by pregnant women in Health Center - Mukalla Directorate - Yemen were summarized in **figures (5, 6).**

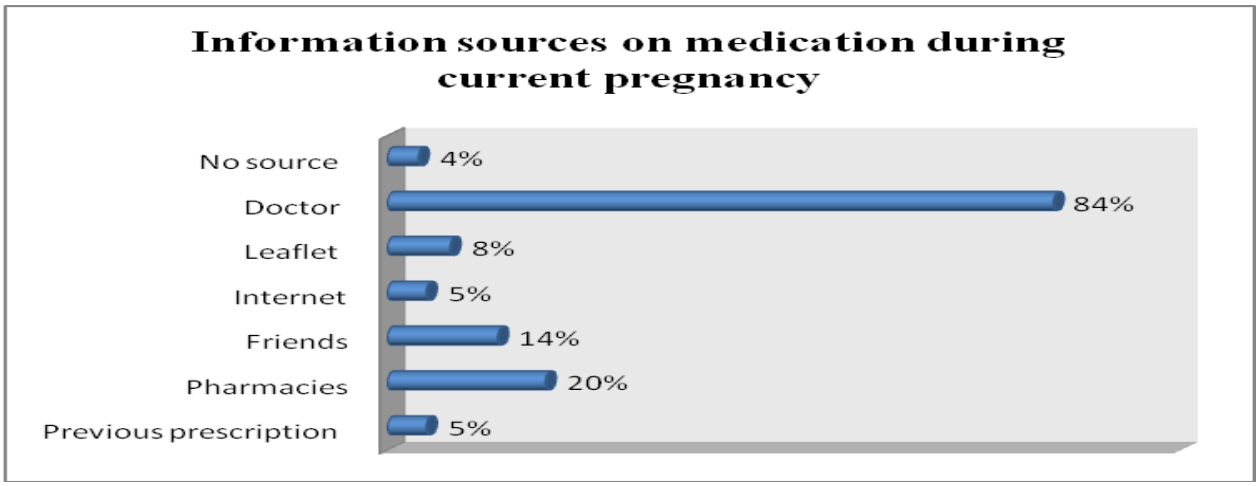

Figure (1): Information sources of medication during the current pregnancy

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Table (1) : Socio-demographic characteristics of participants.

Characteristics 1-Personal Data:	Limits	Total respondents	
		Number of cases	Percentage
Age Range(Years)	15-24 years	168	42%
	25-35 years	184	**46%**
	36-45 years	36	9%
	>45 years	12	3%
Education level	No formal education or elementary school	84	21%
	Middle school	144	**36%**
	High school	112	28%
	College degree or higher	60	15%
Occupation	House-wife	320	**80%**
	Student	20	5%
	Health-related career employee	4	1%
	Other employees	56	14%
2- Self-perceived health status:			
No. of pregnancy	**First One**	168	**42 %**
	Second One	96	24%
	More than 3	136	34%
Medications used during pregnancy	**Yes**	208	**52%**
	No	192	48%
Trimester of medication used	First	100	25%
	Second	152	**38%**
	Third	148	37%
Chronic disease	Yes	24	**6%**
	No	376	94%
Drugs used in Chronic disease after pregnancy	No	12	**3%**
	Change the drug of chronic disease	28	7%
	Consulted a doctor	348	87%
Congenital malformation	No	388	97%
	Yes	12	**3%**

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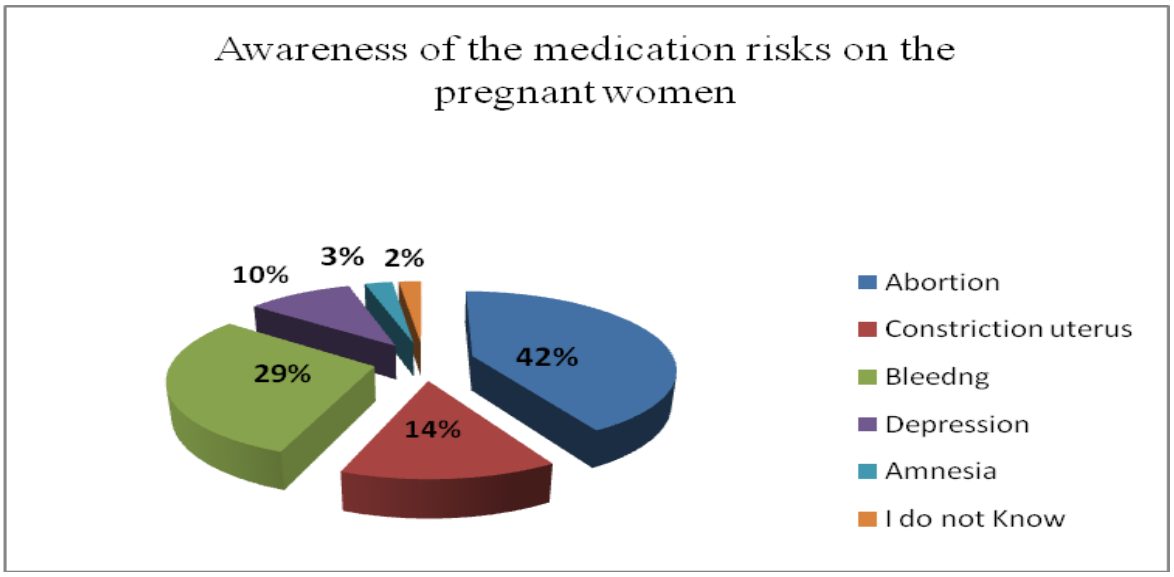

Figure (2): Awareness of the medication risks on the pregnant women

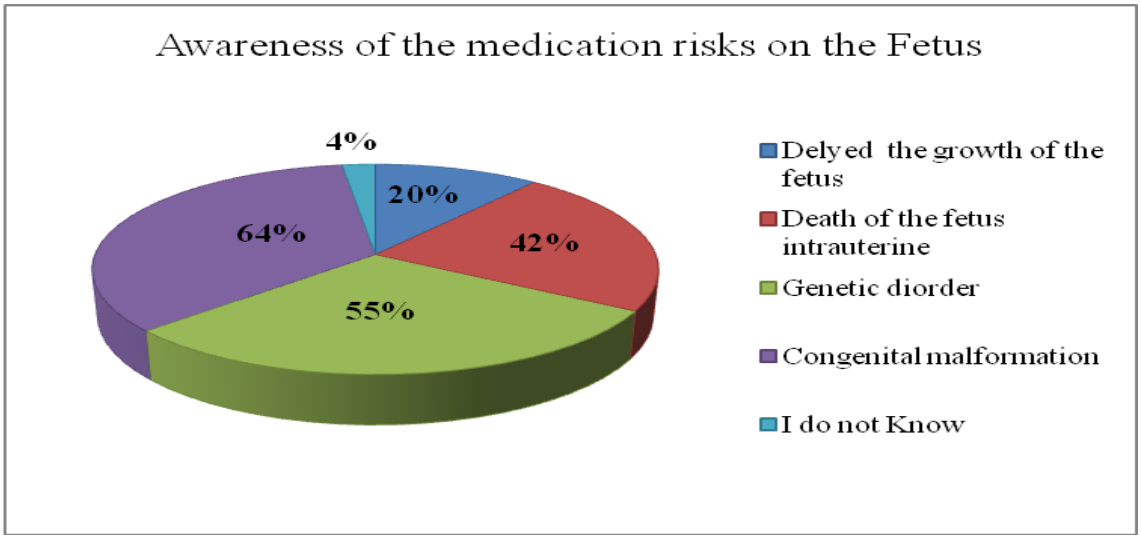

Figure (3): Awareness of the medication risks on the fetus

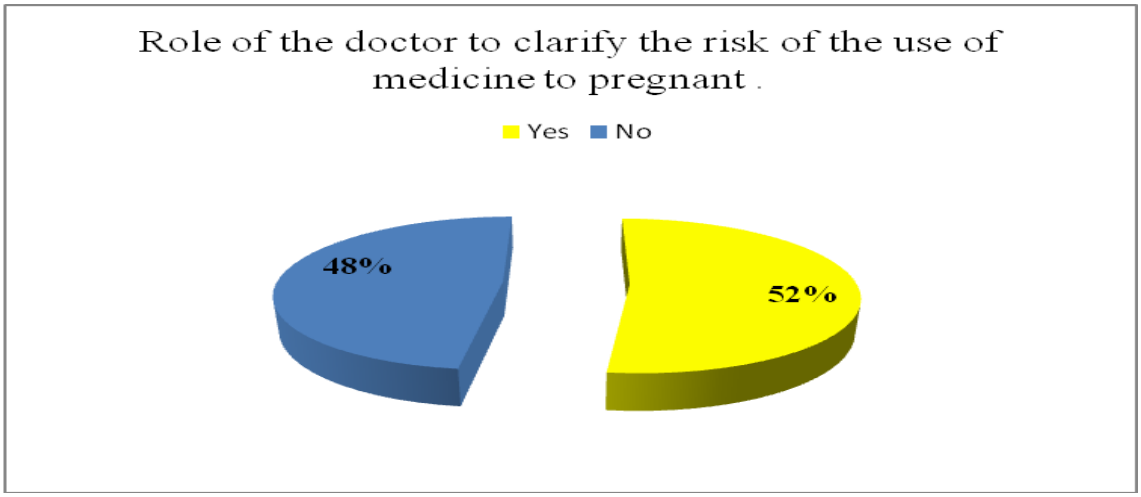

Figure (4): Role of the doctor to clarify the risk of the use of medicine to pregnant women

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Table (2): Pregnant women's beliefs (Attitude) about medication use during the current pregnancy

Statement	Yes		No		I don't know	
	.Freq	%	.Freq	%	Freq	%
• Doctors prescribe too many medicines	100	**25%**	256	64%	44	11%
• All medicines can be harmful to the fetus	44	**11%**	320	80%	36	**9%**
• Natural remedies can generally be used by pregnant women	216	**54%**	140	35%	44	11%
• It is better for the fetus that I use medicines and gets well than to have untreated illness during pregnancy	332	83%	48	**12%**	20	5%
• Most medicines are addictive	184	**46%**	120	30%	96	**24%**
• Natural remedies are safer than medicines	192	**48%**	152	38%	48	12%
• Drink vitamins and drugs may increase fetus size and difficult delivery	236	**59%**	100	25%	64	16%

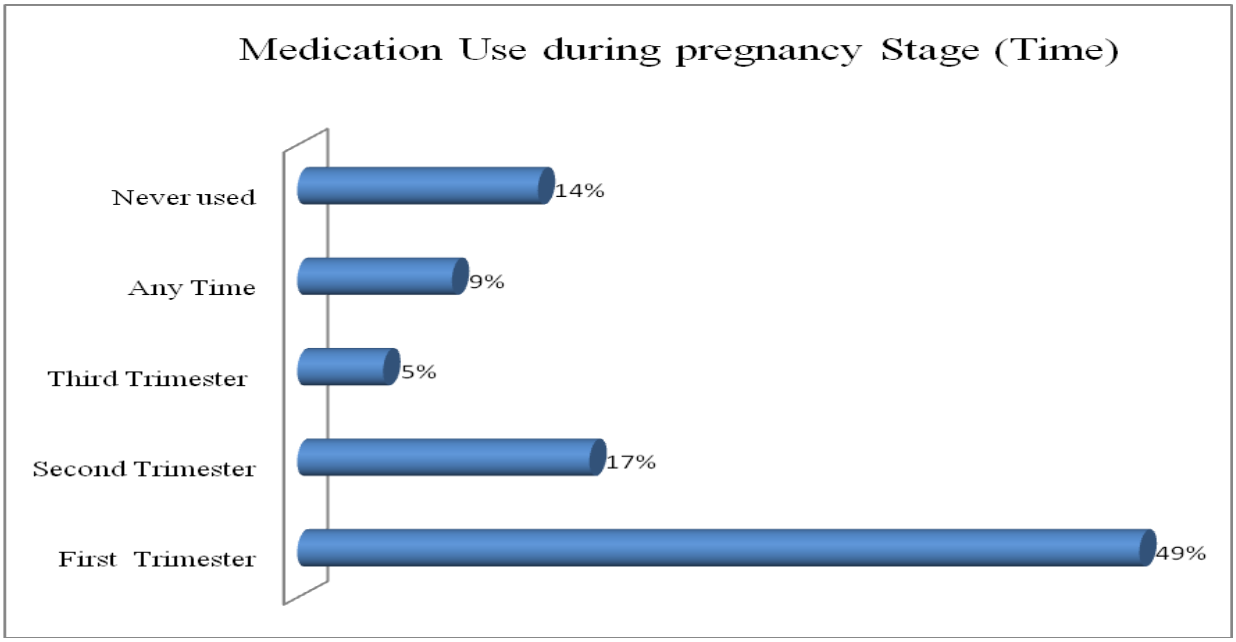

Figure (5): Medication Use during Pregnancy Stage (Time)

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Discussion:

Pregnancy is a special physiological state where medication intake presents a challenge and a concern due to altered drug pharmacokinetics and drug crossing the placenta possibly treatment in pregnancy cannot be totally avoided, since some pregnant women may have chronic pathological conditions that require continuous or interrupted treatment causing harm to the fetus (11). Four hundred respondents were approached for participation. All of them provided complete information. In our study, the majority percentage of the age was between (25-35) years. But according to the level of education, Middle school was the higher percentage, and the majority percentage of Occupations was House-wife. On the Other hand, Heath stated characteristics of the respondents the first pregnancy was the majority percentage of the Number of pregnancies, In our study we found that the prevalence of medications used during the current pregnancy was more than half of pregnant women, and medications were commonly used in the second, and third trimesters, these results disagree of AbdElrahium study results in Sudan,(2013) which was the third trimester most trimester used the drugs (12)We found also that 6% of pregnant women had chronic disease and 3% did not change the drugs of chronic disease after pregnancy. Also, we found 3% of our respondents had congenital malformation (12).

The most common source of updated knowledge about drug information among pregnant women in the University of Medical Center - Mukalla Directorate- Yemen in our study was from doctors and a pharmacist but 5% of the participants reported that they hadn't any source of information about drugs. This result agrees with the study by Noha M. et (2014) in Saudi Arabian reported that the source of updated knowledge about drug information was the doctor. (13). In our study, we noted that the role of the doctor is to clarify the risk of medication used during pregnancy, but nearly half of the doctors did not explain the risk to them, This result disagrees with a study by Noha M. et (2014) in Saudi Arabian reported that doctors give complete information about the drugs to the pregnant women (13). On the other hand, the majority percentage of the awareness of medication risks on pregnant women and fetuses were abortions on pregnant women and congenital malformation in the fetus but pregnant women did not know any information about the risk of drugs during pregnancy or on the fetus, this result agrees with the study by Monica Navaro, et (2018). Italy's study reported that awareness of medication risks for pregnant women and fetuses was lacking on some points (14).

In our results, we found the negative pregnant beliefs about medications were that the doctors prescribed too many medicines, most medicines are addictive's, natural remedies are safer than medicines, and drinking vitamins and drugs may increase fetus size and difficult delivery, this result agrees with a study by Noha M. et (2014) in Saudi Arabian reported negative beliefs about medications (15).

Finally, from our study, we reported that the most common medications used were vitamins, followed by antibiotics prescribed to pregnant women. All drugs used by pregnant women at the University of Medical Center Mukalla Directorate - Yemen The results of our study agree of the most common medication used was vitamins to study done in Sudan (AbdElrahium D. et), study (2015) (15).

Conclusions:

The present study indicates that the prevalence of drugs used during pregnancy was mainly vitamins and antibiotics were used, On the other hand, the doctors didn't play a positive role to clarify the risk of the use of medicine by pregnant women or

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fetuses correctly. Although doctors and pharmacists were the main sources of information for pregnant women. Also, we found that the Drink vitamins and drugs may increase fetus size and difficult delivery" was the opinion of most pregnant women. It is therefore an urgent need to make them aware of the risks of drugs to ensure the safe use of medicines for pregnant women and fetuses.

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Evaluation of Serum Electrolytes Disturbances among Type 2 Diabetes Mellitus Patients in Dhamar, Yemen.

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Article Info:

Article type:
Research Article
Received:
13 March 2023
Revised:
03 April 2023
Accepted:
24 May 2023

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Conflict of interest: Nil

Al-Saeeda Journal of Medical Sciences (SJMS)

ISSN: 2710-4877 (Print); ISSN: 27104885 (Online)

Available Online at: journal.su-edu.net/index.php/su-journal

A peer reviewed medical journal published by Faculty of Medical Sciences - Al-Saeeda University, Dhamar, Yemen

SJMS; Volume 5, Issue 1; May: 2023; Page No. 26-36

Evaluation of Serum Electrolytes Disturbances among Type 2 Diabetes Mellitus Patients in Dhamar, Yemen.

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Article Info:

Article type:
Research Article

Received:
13 March 2023

Revised:
03 April 2023

Accepted:
24 April 2023

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Conflict of interest: Nil

To cite this article:
Abdulqawi Ali Al-Shammakh1*, Abdulrahman H Amer, et.al, Evaluation of Serum Electrolytes Disturbances among Type 2 Diabetes Mellitus Patients in Dhamar, Yemen. *SJMS*. (2023).; 5(1):P. 26-36.

Abstract:

Background: Diabetes is one of the diseases which frequently lead to electrolyte distortion. **Aim**: This study was conducted to evaluate the electrolytes disturbances and associated risk factors in type 2 diabetes mellitus patients. **Methodology:** A Case-control study was conducted on 70 type 2 diabetes mellitus patients and 70 apparently healthy persons in Dhamar city. Data were collected using questionnaires, sociodemographic and clinical data were reported through direct interview. Anthropometric measurements were estimated in the hospital during interview. Blood samples for estimation of glucose and electrolytes were collected from all participants after overnight fasting state. Laboratory measurement for glucose, sodium, potassium, calcium and magnesium were carried out using commercial kits. Data were analysis using SPSS and p value of <0.05 was assumed significant **Results**: In this study, the control group had 34% males and 65.7% women, while the diabetes group included 68.9% men. Diabetics had higher serum potassium and calcium levels, with a higher prevalence of hypernatremia (18.9% vs. 1.4%), hyperkalaemia (41.9% vs. 2.9%), and hypermagnesemia (9.5% vs. 2.9%) compared to controls. The study found that patients with FBS levels above 130 mg/dl, patients over 40 years of age, male subjects and hypertensive patients had significantly higher serum potassium levels. Patients with FBS values over 130 mg/dl and patients with high blood pressure also had significantly higher sodium concentrations. Increased age is positively correlated with FBS and potassium levels, while magnesium and BMI show negative correlations. There are positive correlations between magnesium, calcium and potassium. **Conclusion:** Diabetic patients have a higher prevalence of electrolyte imbalance, possibly due to glucose homeostasis dysregulation. Future research is needed to establish a reference interval for electrolytes in adult Yemeni populations.

Keywords: Yemeni, Diabetics, Electrolyte imbalances

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Introduction:

Diabetes has become increasingly prevalent worldwide and is now recognized as one of the most widespread noncommunicable diseases. According to the latest edition of the IDF Diabetes Atlas for the year 2021, an alarming 10.5% of adults aged between 20 and 79 years worldwide are currently grappling with diabetes. What's more concerning is that nearly half of these individuals are oblivious to their diabetic status, living with the condition unknowingly (1).

Numerous studies and investigations have consistently highlighted the alarming fact that diabetes is a leading cause of a variety of serious health complications including blindness, kidney failure, heart attacks, stroke and the unfortunate need for lower limb amputation (2,3).

Electrolytes are crucial for maintaining normal cell function and conducting nerve and muscle activity. Important electrolytes include sodium, potassium, chloride, magnesium, calcium, phosphate, and bicarbonates (4). Diabetes can cause metabolic imbalance and disruptions in electrolyte concentration, which can have a significant impact on the body. The cause is usually multifactorial, but usually results from insulin deficiency or insulin resistance, diabetic ketoacidosis and hyperglycaemias (5). The mechanism of electrolytes changes involves osmotic effect of hyperglycaemias, distribution of water movement between intra and extracellular compartments, and the activity of Na+/K+ ATPase pump. Insufficient insulin production or insulin resistance can lead to reduced activity of a transporter protein that maintains the balance of sodium and potassium concentration. This can result in changes in electrical gradients and further affect electrolytes levels (5,6). The most common pattern of electrolytes disturbances in diabetic patients are, hyponatremia, hypomagnesemia,hypocalcaemia, and dyskalaemia (7). Hyperkalaemia is more common in diabetic patients compared to the general population (7,8). This can occur when potassium moves from inside the cells to the outside, causing an increase in potassium levels without an overall increase in the body's total potassium. Acidosis, insulin deficiency, hypertonicity, cell breakdown, and certain medications like beta blockers can all contribute to this type of hyperkalaemia in diabetes (6,8). On the other hands hypokalaemia in diabetics was reported in several studies (7,10) which could be attributed to shift hypokalaemia due to insulin administration, renal loss of potassium ions due to osmotic diuresis, Hypomagnesemia which lead to activates the renal outer medullary potassium ions channel to secrete more potassium ions (10).

Since the electrolytes play a crucial role in maintaining normal physiological function. Imbalances in these electrolytes can have neurological and cardiac effects such as seizures and abnormal heart rhythms. Bicarbonate imbalance can also lead to metabolic acidosis or alkalosis. In diabetics, these predictions should not be taken lightly as they highlight the urgent need for increased awareness, prevention and treatment of electrolyte imbalances. Furthermore, like others in Yemen, diabetics suffer from lack of health care, economic problems and poor education, making it impossible for them to properly assess their clinical situation on a regular basis. In addition, there is very limited research on this topic in diabetics. Therefore, this study aimed to evaluate the electrolyte imbalances in diabetics.

MATERIALS AND METHODS

Study design and population:

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A Case-control study was conducted on 70 type 2 diabetes mellitus patients and 70 apparently healthy persons attending Dahmar General Hospital Commission in Dhamar city. The sample size was calculated based on the power (1-beta) = 0.8, the ratio of the sample size, control/case = 1, the event probability in the case group = 0.83 and the event probability in the control group = 0.52 over the previous determined study and 2-sided significance level = 0.05 (11). The sample size was 41 for the control group and 41 for the case group. Because the estimate was for overall electrolyte imbalance and the variability was high for certain electrolytes, we increased the sample size to 70 for both groups.

Data were collected using questionnaires, and sociodemographic and clinical data were reported through face-to-face interviews. During the interview, anthropometric measurements and physical examinations were performed in the hospital. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in the right arm after 15 minutes of rest in a sitting position.

Laboratory tests:

Venous blood samples were taken from all subjects after an 8-12-hour overnight fast and transported to the laboratory for testing. Serum levels of glucose and electrolytes, including sodium, potassium, calcium and magnesium, were estimated spectrophotometrically using commercially available kits.

Parameters definition:

The electrolyte imbalances were defined based on the reference intervals for each electrolyte as follows: sodium (135–145 mmol/l), potassium (3.5–5.0 mmol/l), magnesium (1.7–2.8 mg/dL), and calcium (8.0–10.4 mg/dl). Values above or below these ranges for each individual electrolyte were considered hypo or hyper. FBS was defined as a poor control at a level of 130 mg/dl (16). BMI was classified as overweight or obese (BMI 25.0 kg/m2) and not overweight (BMI <25.0 kg/m2) (37). Hypertension is defined as a systolic blood pressure (SBP) of 140 mm Hg, diastolic blood pressure (DBP) of 90 mm Hg, or self-reported use of antihypertensive medication (16).

Data analysis:

The data were analysed with SPSS 22. Categorical data were presented as frequency and percentage. FBS and electrolyte values were expressed as mean with standard deviation. The t-test was used to compare the mean of FBS and electrolytes in controls and diabetics. A correlation study was conducted between electrolytes and glucose, BMI and age. p-values less than or equal to 0.05 were considered statistically significant.

RESULTS

General characteristics of the study population

The characteristics of the study population are presented in Table 3:1. In this study, most of the diabetic participants were over the age of 40. The distribution of gender between the control and diabetic groups was 34% male, 65.7% female for the control group and 68.9% male, 31.1% female for the diabetic group. Approximately 64.9% of the diabetics had a BMI higher than 25 kg/m2, compared to 35.1% in the control group. The majority of participants in this study were unemployed. Around half of the study population had a family history of diabetes. More than two-thirds of the diabetics followed a diet, while only 1.4% of the control subjects were on a diet.

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Table 1. General characteristics of the study population

Parameters		Control subject	Diabetic subjects
Age year	>40	10 (14.3%)	65 (87.8%)
	≤40	60(85.7%)	9 (12.2%)
BMI kg/m2	<25	50 (71.4%)	20 (28.6%)
	≥25	26 (35.1%)	48 (64.9%
Sex	M	24 (34.3%)	51(68.9%)
	F	46(65.7%)	32 (31.1%)
Occupation	Employed	22 (31.4%)	25 (33.8%)
	Unemployed	48(68.6%)	49 (66.2%)
Family history of T2DM	Yes	34 (48.6%)	43 (58.9%)
	No	36 (51.4%)	30 (41.1%)
Hypertension	Yes	2 (2.9%)	34 (45.9%)
	No	68 (97.1%)	40 (54.1%)
Kidney	yes	32 (45.7%)	52 (70.3%)
	No	38 (54.3%)	22 (29.7%)
Eye	Yes	2 (2.9%)	30 (40.5%)
	No	68 (97.1%)	44 (59.5%)
Diet	No	69 (98.6%)	23 (31.1%)
	Yes	1 (1.4%)	51 (68.9%)

Levels of glucose and electrolytes in diabetic and control subjects

The differences of FBS and electrolytes mean levels in diabetic patients and control were shown in table 2. The result indicated that FBS, serum potassium, and calcium levels in diabetic patients were significantly higher than control ($p < 0.05$). Serum sodium and magnesium levels were also slightly increased in diabetic patients compare to control, but without statistical significances.

Table 2. Levels of glucose and electrolytes in diabetic and control subjects

Parameters	Subjects	N	Mean	Std. Deviation	P value
FBS mg/dl	**Diabetes**	74	193.70	74.87	0.000
	Control	70	97.41	11.21	
K mmol/l	**Diabetes**	74	4.70	0.780	0.000
	control	70	4.10	0.49	
Na mmol/l	**Diabetes**	74	137.20	10.62	0.153
	control	70	135.10	5.90	
Mg Mg/dl	**Diabetes**	74	1.70	0.44	0.254
	control	70	1.60	0.29	
Ca mg/dl	**Diabetes**	74	8.6	1.00	0.044
	control	70	8.30	0.88	

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Serum Levels of FBS and electrolytes based on population characteristics

The levels of FBS and electrolytes based on populations characters are shown in table 3. FBS was found to be high in male patients, subject with age over 40 years, patient had no diet adherence, and hypertensive patients. The result of this study also indicated that High sodium concentration found in patient with FBS over 130 mg/dl (*P* 0.002) and patient with hyper tension (*P* 0.064). According to gender, age over 40 years and BMI over 25 kg/m2 concentration of sodium was not significantly differed. On the other hand, serum potassium was significantly higher in male (*P* 0.002), age over 40 years (*P* 0.000), patients with FBS more than 130 mg/dl (*P* 0.001), hypertensive patients (*P* 0.000) and in subjects who had no diet (P 0.000), While the serum calcium and magnesium were not significantly changing according to the categories of age, BMI, FBS and hypertension, significant differences in the levels of calcium was found between male and female (p 0.006).

Table 3. Serum Levels of FBS and electrolytes based on population characteristics

Characters	Category	**No**	**Mean ± Standard deviation**				
			FBS mg/dl	**Na+ mmol/l**	**K+ mmol/l**	**Mg++ mg/dl**	**Ca++ mg/dl**
Gender	M	75	165.74 ±78.54	136.94 ± 8.86	4.60 ±0.73	1.72 ± 0.42	8.70 ± 0.94
	F	69	126.41 ± 59.32	135.40 ± 8.50	4.21 ± 0.66	1.63 ± 0.36	8.21 ± 0.92
	P		0.001	0.289	0.002	0.184	0.006
Age	>40	75	182.70 ± 78.52	136.70 ±10.70	4.63 ±0.80	1.70± 0.42	8.5 ± 1.0
	≤40	69	108.01 ± 37.33	135.70± 5.70	4.20 ±0.52	1.70 ±0.33	8.4±0.90
	p		0.000	0.475	0.000	0.690	0.693
BMI kg/m2	≥25	68	153.60 ± 63.60	135.60 ± 9.22	4.34± 0.75	1.61 ± 0.41	8.50 ±1.04
	<25	76	140.92 ±79.60	136.80 ± 8.20	4.50± 0.69	1.73 ± 0.33	8.40 ± 0.88
	p		0.297	0.420	0.343	0.050	0.644
FBS mg/dl	≥ 130	38	215.45± 68.05	138.19± 10.52	4.64 ± 0.80	1.73 ± 0.46	8.60 ± 1.2
	<130	106	99.31 ± 12.26	134.83± 6.88	4.23 ± 0.64	1.64 ± 0.31	8.40 ± 0.94
	p		0.000	0.002	0.001	0.177	0.207
Hypertension	Yes	36	167.90 ± 64.42	138.52 ±10.60	4.82 ± 0.80	1.64 ± 0.41	8.60 ± 1.12
	No	108	139.90 ± 73.94	135.43 ± 7.90	4.30 ± 0.64	1.70 ± 0.37	8.40 ± 0.89
	P		0.045	0.064	0.000	0.534	0.245
Diet	*No*	69	182.66 ± 78.53	136.71± 10.73	4.60 ± 0.80	1.69 ±0.42	8.50±1.0
	Yes	75	108.01± 37.33	135.66 ± 5.73	4.20 ± 0.53	1.66±0.33	8.40±0.90
	P		0.000	0.470	0.000	0.690	0.693

Frequencies of abnormal levels of electrolytes among diabetics and control subjects

The frequencies of abnormal levels of sodium, potassium, magnesium and calcium are shown in table 4. The result indicated that patients with diabetes mellitus had higher frequencies of abnormal high levels of sodium (18.9%) potassium (41.9%), magnesium (9.5%) than control. Abnormal high levels of magnesium and calcium were also found in diabetic patients more than control. Normal levels of sodium and potassium were found in 40.5% and 50 % of diabetic patients which is lower that of the control 58.6% and 88.6%. The distribution of low levels of sodium, potassium, magnesium, and calcium in diabetic patients were found to be not much different from those in the control.

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Table 4: Frequencies of abnormal levels of electrolytes among diabetics and control subjects

Parameters		Diabetic patients Frequencies (%)	Control Frequencies (%)
Na	**Normal**	30 (40.5%)	41(58.6%)
	High	14 (18.9%)	1 (1.4%)
	Low	30 (40.5%)	28 (40 %)
K	**Normal**	37 (50 %)	62 (88.6%)
	High	31(41.9%)	2 (2.9%)
	Low	6 (8.1%)	6 (8.6%)
Mg	**Normal**	29 (39.2%)	29 (41.4%)
	High	7 (9.5%)	2(2.9%)
	Low	38 (51.4%)	39 (55.7%)
Ca	**low**	21 (28.4%)	26 (37.1%)
	Normal	51 (68.9%)	44 (62.9%)
	High	2 (2.7%)	0 (0.0%)

Correlation of age, BMI, FBS and electrolytes

Correlation analysis (table:5) revealed that increased age was positively correlated with levels of FBS (r= 0.561**) and potassium (r= 0.322**). Increased levels of FBS were correlated with higher serum potassium concentration (r=0.318**). We found no significant correlation between levels of FBS and sodium, calcium, and magnesium. Magnesium and BMI was found to be negatively correlated while there was positive correlation between magnesium with calcium (r=0.265**) and potassium (r=0.162). There was a positive correlation between potassium and calcium (r=0.294**). No correlation was found between sodium with magnesium, and calcium.

Table 5. Correlation of age, BMI, FBS and electrolytes

Parameter	Pearson Correlation (r)	Significance	
Age & FBS	0.561**	0.000	
AGE & K	0.322**	0.000	
BMI & mg++	-0.224**	0.007	
FBS & Na	0.141	0.092	
FBS & K	0.318**	0.000	
FBS & Ca	0.135	0.106	
FBS & Mg	0.061	0.466	
Na & K	0.090	0.248	
K & Ca	0.294**	0.000	
Na & Mg	0.040	0.617	
Mg &Ca	0.265**	0.001	
Mg & K	0.162	0.052	
**. Correlation is significant at the 0.01 level (2-tailed).			

DISCUSSION

Diabetics are more prone to developing electrolyte imbalance (ED) due to various mechanisms including hyperglycaemia-induced osmotic fluid shifts or by osmotic diuresis, cell shifts from intracellular to extracellular space, from extracellular to intracellular space, caused by insulin deficiency or insulin administration, diabetic ketoacidosis. Metabolic acidosis and

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associated diabetic chronic kidney disease (5,6,7). The main purpose of the work was to draw attention to the electrolyte imbalances in type 2 diabetes mellitus in the city of Dhamar.

Our results describe the concentration of electrolytes both in the control group and in the diabetic group (Table 3.2). Diabetics had significantly higher serum potassium and calcium levels compared to controls ($p<0.05$). Conversely, diabetics also had slightly elevated serum sodium and magnesium levels compared to controls, but these differences were not statistically significant. The occurrence of diabetes and hyperkalaemia is a well-known phenomenon. The most likely explanation for hyperkalaemia in diabetes is increased potassium release from cells due to intracellular dehydration (12), insulin deficiency leading to inhibition of Na+-K+-ATPase pump function, and decreased maintenance of the intracellular K+ gradient - and extracellular environments (13). In addition, administration of certain medications, such as angiotensin-converting enzyme inhibitors, can decrease potassium secretion from the kidney (14). Hypercalcemia in diabetes has been reported to be associated with dehydration, insulin resistance leading to hyperparathyroidism, inhibition of insulin growth factor 1 by hyperglycaemia, and decreased bone mineralization (15).

Our results indicated an electrolyte abnormality in the diabetic and control groups (Table 3.4). The most common electrolyte disturbances were hyperkalaemia (41.9% vs. 2.9%), hyponatremia (40.5% vs. 40%), hypernatremia (18.9% vs. 1.4%), hypomagnesemia (51.4% vs. 55.7%), hypermagnesemia (9.5% vs. 2.9%). and hypocalcaemia (28.4% vs. 37.1%). The prevalence of hyperkalaemia in our study was higher than in patients enrolled in Ethiopia (9.2%) (16) and southern India (6%) (17). One of the mechanisms of hyperkalaemia is cellular dehydration due to hyperglycaemia, which leads to increased intracellular K+ concentration and favors a gradient for the transport of K+ out of cells. Diabetic nephropathy and hyporeninaemic hypoaldosteronism are commonly observed in people with diabetes (15,18,19,), resulting in decreased glomerular filtration and tubular potassium secretion (15). On the other hand, 8.1% of diabetics were found to have hypokalaemia, consistent with the prevalence of hypokalaemia reported in Thailand (6.7%) and lower than in Ethiopia (22.3%) and India (16,17,20) . The disparity may be due to the diversity of target groups or related to the severity of DM cases. However, this study found that there is no significant difference between the hypokalaemia of diabetic patients and the hypokalaemia of controls. Some factors associated with hypokalaemia in diabetics, such as B. the potassium shift due to insulin administration, potassium loss via the gastrointestinal system, osmotic diuresis and low magnesium levels have also been reported (15).

Hyponatremia in this study (40.5%) was comparable with other studies which carried out in Ethiopia and India which have shown that prevalence of hyponatremia among diabetic patients were 39.2% [95% CI: 31.1–47.9] and 33% respectively (16, 17). Compared to the control group, the frequency of hypernatremia (18.9% vs. 1.4%) was high in our study. Several previous studies reported that the prevalence of hypernatremia in diabetics ranges from 11.4% to 17.3% (16,21,22). The increase in hypernatremia prevalence may be due to the fact that diabetics are more likely to have hyperlipidaemia, which is suspected to reduce plasma water and cause pseudohypernatremia (15). Additionally, some literature reports have found that impaired glucose metabolism due to insulin deficiency and glucagon-induced gluconeogenesis was associated with hypernatremia and hyperosmolarity in human and animal models (15). It is known that hyperglycaemia can change sodium levels in the opposite direction. Therefore, hypernatremia and hyperosmolarity

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should be considered as contributing factors to the occurrence of hyperglycaemia in critically ill patients (23).

Previous research has documented that hypomagnesemia is a common electrolyte abnormality in diabetics (15) and that subjects 55 and older have a high odd of developing hypomagnesemia (OR = 3.32; 95% CI: 2.00–5 .50) (23). In the general population, hypomagnesaemia has been shown to range from 2.5% to 15%, and the prevalence is even higher in critically ill patients, estimated at 65% in one study (25). There are several theories that explain why diabetics often have low levels of magnesium in their bodies. These theories include kidney loss, loss via the gastrointestinal tract, poor diet, excessive filtration in the kidneys, changes in insulin metabolism, use of diuretics, and recurrent metabolic acidosis. It is believed that the main cause of hypomagnesemia in diabetics is osmotic diuresis, which leads to excessive loss of magnesium through the urine (15). Magnesium deficiency has been reported to promote inflammation by disrupting immune function by stimulating phagocytes, increasing granulocyte oxidative burst, activating endothelial cells, and increasing cytokine levels (26). In addition, epidemiological data indicate that patients with serum hypomagnesemia are at increased risk for cardiovascular disease, T2DM, and mortality from these diseases (27).

The increased prevalence of electrolyte imbalances in diabetics and controls, on the other hand, could be due to multifactorial reasons, including geographic characteristics, dietary habits, and food and vegetable availability. In Yemen, it is customary to chew a green leaf called khat. Khat belongs to the Celastraceae family and contains the compounds cathinone and cathine, which are similar to amphetamines. It is believed to be a naturally occurring stimulant derived from the Catha edulis plant and is commonly consumed in Yemen and East African countries (28). An animal study by Limenie et al. (2022) performed on male Swiss albino rats given raw khat extract at doses of 100 mg/kg, 200 mg/kg and 300 mg/kg for 12 weeks found a significant decrease in sodium and calcium concentrations. The K+ concentration was significantly increased in rats receiving raw khat extract 300 mg/kg compared to the control group and in rats receiving raw khat extract 100 mg/kg. Potassium has been found to increase in serum potassium (29).

This study also showed a high prevalence of hypocalcaemia in the diabetic and control groups (28.4% vs. 37.1%). The cut-off we used to define hypocalcaemia in this study was 8.0 mg/dL and hypercalcemia was 10.2 mg/dL. Several factors regulate calcium levels in our bodies, including parathyroid hormone (PTH) and 1,25-dihydroxyvitamin D (1,25[OH]2D) in the kidneys, bones, and gastrointestinal tract (30). So far it has been reported that 18% of all hospitalized patients and 85% of patients in the ICU suffer from hypocalcaemia (31). The prevalence of hypocalcaemia in our study was higher than that reported by Eshetu et al. reported. (15.3%) (15) and lower than Cameron (48%) (33). In contrast, the hypercalcemia in our study (2.7%) was consistent with previous data reporting that the prevalence of hypercalcaemia in hospitalized patients was 2.4% (34) and lower than that reported by Catalano et al., who determined the prevalence of hypercalcaemia 4.74% (35).

According to our results, older age and FBS were positively associated with serum potassium (Table 3.5). This could be related to cellular dehydration caused by hyperglycaemia, insulin deficiency and diabetic nephropathy in the elderly. The negative correlation between BMI and serum magnesium found in our study is consistent with previous findings that hypomagnesemia was associated with a five-fold increased risk of metabolic syndrome and that magnesium levels were negatively correlated with waist circumference and BMI (36). The

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positive correlation between calcium and potassium levels is partially related to hyperglycaemia, cellular dehydration, metabolic acidosis, and insulin resistance (15). In this study, the serum level of magnesium showed a significant positive correlation with the serum calcium level. This association is attributed to magnesium's metabolic role in regulating parathyroid hormone secretion. In addition, low serum Mg2+ levels can secondarily trigger hypokalaemia, hypocalcaemia, and hypophosphatemia, which may be further related to the long-term complications of DM (15).

Although this study provides innovative information on electrolyte imbalances, the analysis does not allow us to determine the cause of electrolyte imbalances in patients and controls. Some other electrolytes such as chloride and phosphorus were not considered in this study.

Conclusion: Diabetic individuals had a much greater prevalence of electrolyte abnormalities. According to this study, electrolyte imbalance in diabetes patients may be caused by disruption of glucose homeostasis. The high prevalence of low electrolytes levels in healthy participants highlights the need for more study to develop an adult Yemeni population electrolyte reference interval that is really future-proof.

Acknowledgment

The authors are grateful to the director and physicians of Dhamar General Hospital Commission. We would like to acknowledge the Department of Medical laboratory, Faculty of Medical Science Al-Saeeda University. We acknowledge all the participants for their voluntary involvement in this study.

Author Contributions:

Abdulqawi A. A. and Abdulrahman A. and designed the study. The remaining authors participated in data collection, sampling and conducting the laboratory experiments. Abdulqawi A.A. took the lead in writing the manuscript. Abdulrahman A. contributed to the discussion and interpretation of the results. All authors reviewed the results and approved the final version of the manuscript.

Conflicts of Interest:

All authors declare no conflicts of interest.

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Antibiotics Susceptibility of Staphylococcus Aureus Isolated from Different Samples in some Medical Laboratories (Thamar City-Yemen).

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Article Info :

Article type:
Research Article
Received:
30 February 2023
Revised:
05 April 2023
Accepted:
22 April 2023

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Conflict of interest: Nil

Al-Saeeda Journal of Medical Sciences (SJMS)

ISSN: 2710-4877 (Print); ISSN: 27104885 (Online)

Available Online at: journal.su-edu.net/index.php/su-journal

A peer reviewed medical journal published by Faculty of Medical Sciences - Al-Saeeda University, Dhamar, Yemen

SJMS; Volume 5, Issue 1; May: 2023; Page No. 36-45

Antibiotics Susceptibility of Staphylococcus Aureus Isolated from Different Samples in some Medical Laboratories (Thamar City-Yemen).

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Article Info:
Article type:
Research Article
Received:
30 February 2023
Revised:
05 April 2023
Accepted:
22 April 2023
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Conflict of interest: Nil

To cite this article:
Ahmed Al-Washli, Salah Aldeen Alhaidary, Ahmed G. Al – Akydy, Samir Alsenafy, Antibiotics Susceptibility of Staphylococcus Aureus Isolated from Different Samples in some Medical Laboratories (Thamar City-Yemen).. *SJMS*. (2023).; 5(1):P. 36-45.

Abstract:

The importance of *Staphylococcus aureus*, as a persistent nosocomial and community-acquired pathogen, has become a global health concern. It has a remarkable capability of evolving different mechanisms of resistance to most antimicrobial agents. The aim of the present study was to evaluate the antimicrobial resistance as well as the prevalence of antibiotic resistant *Staphylococcus aureus* in various clinical samples. Two hundred and thirty-eight samples of S. *aureus* obtained from various clinical specimens between January and June 2018 from six laboratories and two hospitals, in Thamar city. In this study, the *S. aureus* was the most common in age group (21-40 years), the pus sample represented the highest source of *S. aureus* isolated with 31.51%. *S. aureus* was highest sensitivity to Piperacillin, Levofloxacin, Doxycycline, Ciprofloxacin and Amikacin, (89.66%, 83.54%, 69.75%. 67.9% and 65.49%, respectively), whereas, it was the highest resistant to Ampicillin, Cefdinir, Amoxicillin, Lincomycin and ceftazidime (100%, 100%, 76.27%, 74.44%, and 53.19% respectively). Most of antibiotics which reveled high sensitivity to *S. aureus* as Levofloxacin, Doxycycline, Ofloxacin and Piperacillin not used in most Culture\Sensitive test in some laboratories.

Keywords: Key words: Antibiotic, *Staphylococcus aureus*, Sensitivity, Resistant.

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Introduction:

Staphylococcus aureus is gram-positive bacteria spherical cocci, arranged characteristically in grape-like Clusters, they are non sporing, non-motile, catalase positive and usually non capsulate with the exception of rare strains. *S. aureus* measuring about (0.5–1.0) m in diameter **(Cheesbrough, 2006; Kumar, 2016)**. It is facultative anaerobic in nature and is normal commensal on skin and in nasal passage. It is the common cause of purulent infections including boils, carbuncles, furuncles, sinusitis, otitis media, food poisoning, osteomyelitis, pneumonia and sepsis **(Kumar, 2013)**.

Resistance to commonly used antimicrobial drugs is frequently encountered with S. aureus. Some of the mechanisms in resistance include; inactivation of antibiotics by the enzymes, decreased affinity for the antibiotics caused by alteration of the target, efflux pumps, and trapping of the antibiotic **(Pantosti A and Sanchini A, 2007)** . Antibiotic resistance leads to prolonged hospital stay and increased costs in terms of treatment. In addition to these, it causes life threatening infections such as in cases of pyomyositis and chronic osteomyelitis **(Kitara LD et ali, 2011).**

The problem with *Staphylococcus aureus* became more complicated when it was found that it quickly developed resistance and was capable of producing many antibiotic resistant strains. (**Kitara LD et ali., 2011**). The aim of the present study was to evaluate the antimicrobial resistance as well as the prevalence of antibiotic resistant *Staphylococcus aureus* in various clinical samples.

Materials and methods

Timing and Area of Study

This is a descriptive study of previous archived data from (JAN-JUN / 2018). It was taken from six laboratories and two hospitals in Thamar city, Yemen.

Population, Sampling and Participants:

All patients who were infected with bacteria and did not have a pre-response to the medicine were asked to do a Culture\Sensitive (C\S) test. The number of samples that were collected from various clinical samples were 576. They had been being collected out of eight biological laboratories for six months. The sample data were collected from targeted laboratories's test reports of C\S. The reports contain of sex, age, gram stain, specimen, bacteria and antibiotics. Exclusion not all C/S reports contain complete data.

Table1: The targeted laboratories with number of samples

	Laboratories						Hospitals	
	Medlab	Alpha	Alsaeeda	Al-Haya	Al-Jarfi	Al-Dubaee	Al-Mosally	Taiba
Sample	35	82	58	104	34	33	185	45

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Ethical Consideration

This study was based on fully coordination and agreement between the Board of the Faculty of Applied science at Thamar University and the Board of hospitals a5nd Laboratories in question regarding providing us with information and reports in a voluntary manner; no problem if the actual names and details were deleted from reports for Privacy affairs.

The Statistical Analysis

These reports involved some information like Age, Sex, Specimen, Bacteria and Antibiotics, and was scheduled by IBM SPSS Statistic 22 software (Analyze, descriptive Statistics, frequency and percentage).

Results

The present cross-sectional study was conducted upon 576 clinical samples found in Thamar city. The most prevalent bacteria among all clinical samples was *Staphylococcus aureus*, and the most prevalent was pus and urine specimens. Concerning *S. aureus*, susceptibility was found for many antibiotics as Ofloxacin and Ciprofloxacin. Piperacillin was highly sensitive, while Ampicillin and Cefdinir were highly resistant. The details are shown in the figures below.

Prevalence of Pathogenic Bacteria in Thamar City

A total of 576 clinical samples analyze for 6 months. Among the samples, 238 were *S. aureus*, the most prevalent in Thamar city. The results shows the highest percentage for *Staphylococcus aureus* (41.3 %.).

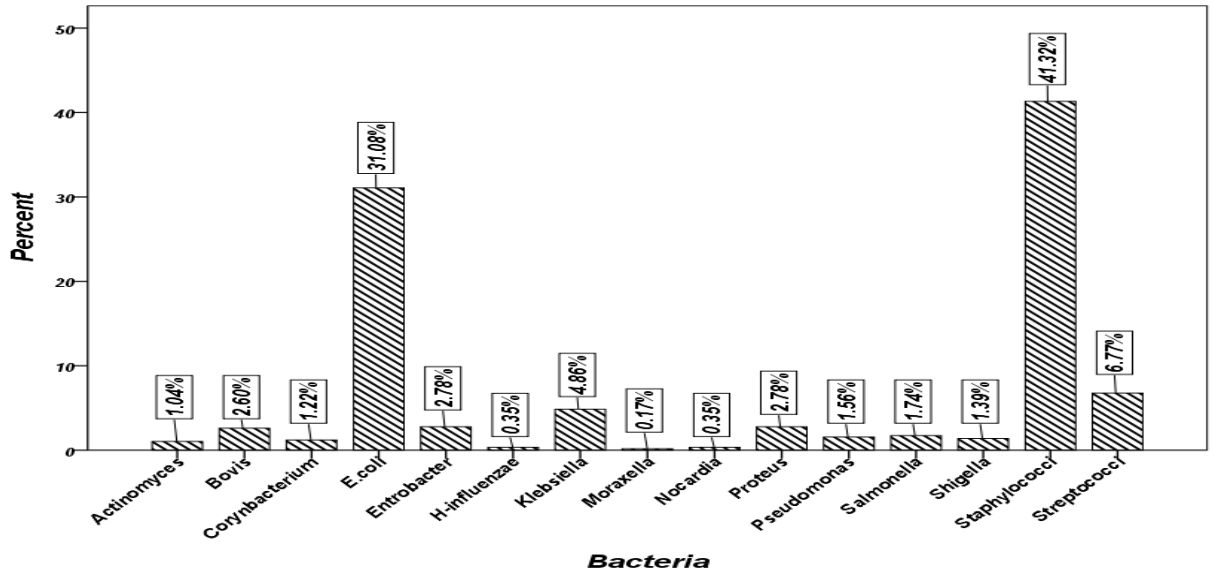

Figure 1: Shows the targeted laboratories with number of samples.

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Distribution of *S. aureus* According to Sex

The result shows that females 121/238 (50 .8%) have higher infection rate than males 117/238 (49.2%).

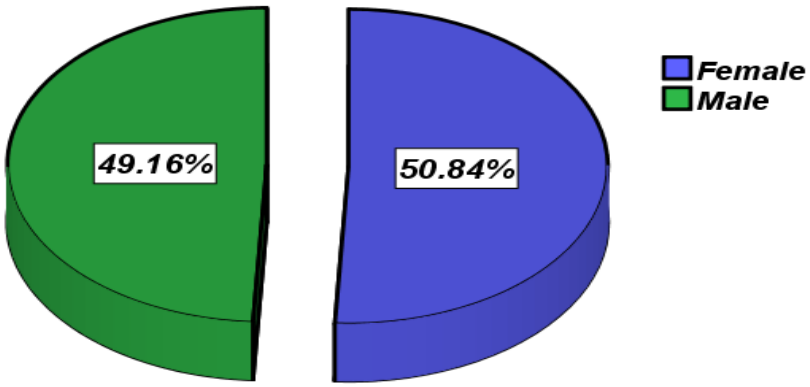

Figure 2: Shows the sex distribution of patients with *S. aureus*.

Distribution of *S. aureus* in Population Based on Age

The results shows that the highest frequency of *S. aureus* occurred in the age group (21-40) years, whereas the lowest was in the age (Over 61) years.

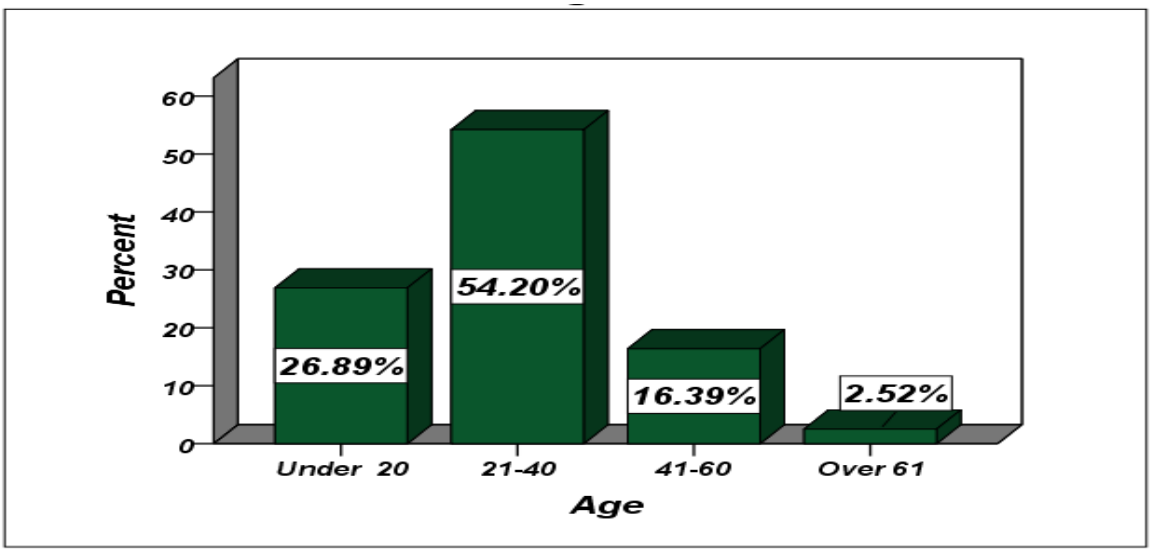

Figure 3: Shows the age distribution of patients with *S. aureus*.

Distribution of *S. aureus* in Population Based on Specimens

The results demonstrate that the highest number of *S .aureu*s was found in pus 75/238 (31.5 %), while the lowest percentage was found in throat, sputum, and pleural 1/238 (0.4%).

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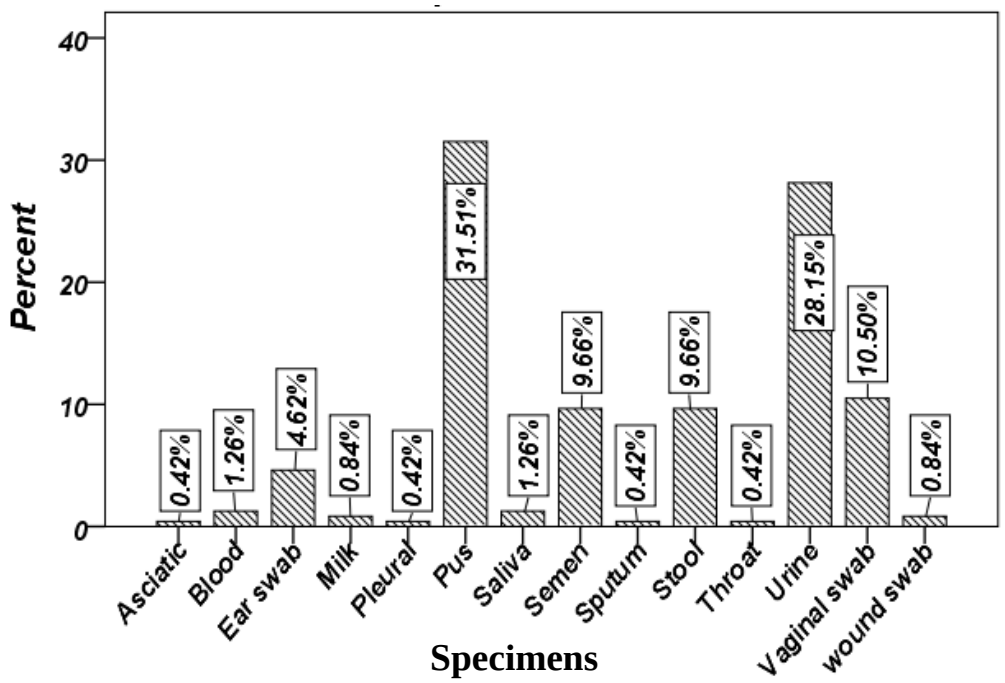

Figure 4: Shows the distribution of *S. aureus* among various clinical sample.

Susceptibility Patterns of *S. aureus*

The study illustrate that 43.15% of *S. aureus* were sensitive to antibiotic, while 32.32% were resistant.

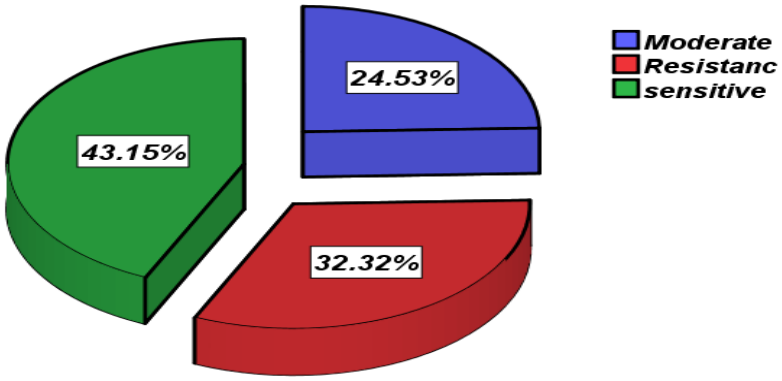

Figure 5: Shows the Susceptibility patterns of S. aureus for antibiotic.

Antibiotics Sensitivity and Resistant to *S. aureus*

The highest frequency of sensitivity observes in Piperacillin (89.66%), followed by Levofloxacin, Doxycycline, and Ciprofloxacin, while the lack antibiotic sensitivity are Amoxicillin, Ampicillin and Cefdinir. The absolute resistant of antibiotics observes in Ampicillin and Cefdinir, while the Piperacillin, Levofloxacin, Ofloxacin and Lomefloxacin were no resistant.

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Table12: Shows the antibiotic sensitivity and resistant of S. aureus to various antibiotics.

Antibiotics Sensitivity		Antibiotics Resistance	
Antibiotics	Percentage	Antibiotics	Percentage
Piperacillin	89.66	Ampicillin	100
Levofloxacin	83.54	Cefdinir	100
Doxycycline	69.75	Amoxicillin	76.27
Ciprofloxacin	67.9	Lincomycin	74.44
Amikacin	65.49	Ceftazidime	53.19
Ofloxacin	60.87	Erythromycin	52.87
Gentamicin	60.47	Amikacin	15.93
Azithromycin	52.86	Ciprofloxacin	14.81
Lomefloxacin	52.17	Gentamicin	13.95
Vancomycin	40	Doxycycline	9.24
Erythromycin	26.44	Azithromycin	5.71
Ceftazidime	21.28	Vancomycin	4
Lincomycin	15.56	Piperacillin	0
Amoxicillin	0	Levofloxacin	0
Ampicillin	0	Ofloxacin	0
Cefdinir	0	Lomefloxacin	0

Discussions

Staphylococcus aureus is a common bacterium colonizing the human skin and mucous membranes. However, *S. aureus* is also a major causative agent of hospital and community-associated infection that can result in life-threatening disease **(Seo *et al.*, 2008; Watanabe *et al.*, 2009)**. Attempts to control the extent of antibiotic-resistant *S. aureus* strains have relied on three factors: ensuring proper hand hygiene among healthcare workers, restricting the use of antibiotics, and promptly identifying and isolates infected patients **(Cooper *et al.*, 2004; Shahmoradi *et al.*, 2019)**.

According to reports collected from some targeted hospitals and laboratories, the percentage of *S. aureus* prevalence is the highest (41.3%) as seen in figure (1). This finding makes the study correspondent to that of a previous study **(Rameshkannan *et al.*, 2014)**, which give percentage of (39%) *S. aureus*.

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The percentage of *S. aureus* prevalence is (49.2%) in males, compared (50.8%) in females, as referred to in figures (2). This result differs from a previous study **(Ayepola *et al.*, 2018)**, which revealed that (52.2%) in males, and (47.8%) in females.

Regarding the " age percentage" in the study, as referred to in figures (3), the age group (21-40) years is highest, with a percentage of (54.20%), whereas the age group (Over 61) years was the lowest, with a percentage of only (2.62%). This result makes the study inconsistent with that in another study carried out by **(Onwubiko and Sadiq, 2011)**, which give percentage of (60%) the age group (Under 20) years, and (23.3%) the age group (21-40) years.

The distribution of *S. aureus* in the clinical samples was high in pus (31.51%), followed urine (28.15%), as shown in figure (4). By this result, the study has a resemblance to that in the previous study by **(Amirmozafari *et al*., 2019)**, which give percentage of 36% and 22.2 for pus and urine, respectively.

The figure (5) of the study, reflected the percentage of "sensitivity of *S. aureus*" was: sensitive (43.15%), moderate (24.53%) and resistance (32.32%), and this is what makes the study corresponding to the study of **(Sebastian *et al.*, 2019)** in the aspect of "sensitivity".

Table (2) of the our study, shown that Piperacillin, Levofloxacin, Doxycycline, Ciprofloxacin and Amikacin, respectively was a highest proportion of sensitivity to *S. aureus*, and, this comes similar with the findings of a previous study carried out by **(Chandrakar *et al.* 2016)**, regarding the proportion of sensitivity to *S. aureus*. However, most of the highly-sensitivity antibiotic were an inhibitor of bacterial protein synthesis and an interference with nucleic acid synthesis. Furthermore, with passing of time, may be reduced little by little until it vanishes at least **(Dionisio *et al*., 2005)**.

A higher sensitivity of Piperacillin was (89.66%), while the resistant was absent in the present study, this result is almost similar with previous study by **(Sebastian *et al.*, 2019),** whereas, the sensitivity in the previous study was (89.00%), while the resistant was (11.00%).

In our results, revealed that the lack resistant for Levofloxacin and high sensitivity 83.54%, in this study was similar with a previous study in Lahore **(Romano and Alfonso, 2004)**, the resistant and sensitivity was 68.13%, 25.5% respectively.

The absolute resistant was represented by Ampicillin, and Cefdinir, and following by Amoxicillin and Lincomycin, this comes similar with the findings of previous study carried out by **(Chandrakar et al., 2016).** Due to the misuse of antibiotics may result in the building up of antimicrobial-resistant bacteria. Uncontrolled selling of antibiotics may be another factor which contributed to the problem

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because antibiotics were being sold in an open and unprotected environment with direct exposure to the sun. this may render the antimicrobials ineffective and, once used for the treatment, expose bacteria to suboptimal concentrations, thereby creating the conditions for the bacteria to develop resistance **(Massawe et al., 2019).**

The our study, showed the high percentage of resistant to Amoxicillin (76%). Whereas, the percentage of sensitivity was non-existent. The Amoxicillin-resistance agreed with a previous study by **(Ahmed *et al*., 2018),** and other study by **(Prasad *et al*., 2018)**, which were 94%, 65.9%, respectively. Furthermore, the lack of antibiotic sensitivity in Thamar city-Yemen, due to unorganized prescription and over the counter handling of antibiotics.

Our study, showed in table (2), point out that, the 100% were Ampicillin-resistant, which agree with previous study in Brazil, at the same percentage by **(Canhas *et al*., 2017)**. This higher resistance of *S. aureus* against penicillins may be attributed to the production of β-lactamase enzyme responsible for inactivation β-lactams which cannot bind to native PBP2A, so synthesis of peptidoglycan and bacterial growth occur normally **(Liu *et al*., 2017; Qayyum *et al*, 2016)**. Our study revealed much higher percentage of Cefdinir-resistant than that reported by **(Canhas *et al*., 2017)**, they found Cefdinir-resistant was 12.50%, which was much lower than our observations, which represented by (100%) of Cefdinir-resistant.

Acknowledgement:

We thank hospital authority and pertinent staff for their support and cooperation. We also thank the students of the year of excellence in faculty of Applied Science -Thamar University (Eman, Fatima, fuad, Ghadeer, Hanan, Hassan, Manal, Naseem, Safa,Shamia, and Zainab)who contribute in collecting data and following the admitted patients.

Conflict of interest:

No conflict of interest associated with this work.

Conclusions

The present study showed that *S. aureus*, was the most common bacteria in clinical specimens. *S. aureus* was most sensitivity to Piperacillin, Levofloxacin, Doxycycline, Ciprofloxacin, Amikacin, Ofloxacin, Gentamicin, Azithromycin, Lomefloxacin and Vancomycin. However, *S. aureus* reveled high resistant to Ampicillin, Cefdinir, Amoxicillin, Lincomycin, Ceftazidime and Erythromycin. Patients with *S. aureus* infection in females have higher rate of infection than that in males. The highest frequency of isolates of S. *aureus*, has accrued in the age group (21-40) years. This study observed a high antibiotic prescription rate by clinicians and that the treatment guidelines for management of patients were not followed. It is notable *S. aureus* was more present in the urinary system because it is more common in the urine sample.

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Volume 5, Issue 1, May 2023