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Full length article

Total Phenolic, Flavonoid Content and Antioxidant Activity of Selected Yemeni Honeys Compared with Manuka Honey

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ABSTRACT

This study evaluated the total phenolic content (TPC), total flavonoid content (TFC), vitamin C concentration, and antioxidant activity (DPPH IC_{50}) in several Yemeni honey varieties, with New Zealand Manuka honey serving as a reference. Five Yemeni honeys were analyzed: Sorab and Acacia from Dhamar governorate, Jaden from Raymah governorate, Sidr from both Dhamar and Hadramout governorates (monofloral), and Maraei from Hadramout governorate (multifloral). Standard analytical methods were employed to determine TPC, TFC, vitamin C, and DPPH IC_{50} values. Results revealed that Yemeni honeys contained TPC ranging from 33.40 to 163.66 mg GAE/100 g, TFC between 1.27 and 4.07 mg QE/100 g, vitamin C levels from 3.29 to 16.32 mg/100 g, and DPPH IC_{50} values between 30.84 and 42.13 mg/ml. In comparison, Manuka honey showed TPC of 108.83 mg GAE/100 g, TFC of 6.07 mg QE/100 g, vitamin C of 10.83 mg/100 g, and the strongest antioxidant activity with the lowest IC_{50} value (11.07 mg/ml). Among the Yemeni samples, Sidr honey exhibited the highest phenolic content (163.66 ± 7.26 mg/100 g) and vitamin C concentration (16.32 ± 0.73 mg/100 g). In conclusion, Yemeni honeys are rich in antioxidant bioactive compounds, underscoring their potential therapeutic value. Future research should expand to other Yemeni honey types and utilize advanced techniques such as HPLC-based profiling to identify individual phenolic constituents.

Keywords: Antioxidant activity, Yemeni honey, DPPH IC_{50}, Vitamin C, Total phenol, Flavonoid, Manuka honey.

INTRODCTION

Honey is a complex natural product containing more than 180 biochemical compounds from diverse molecular families. This mixture is formed after bees process floral nectar within their abdomen (Feknous & Boumendjel, 2022). The physicochemical properties of Yemeni honey are influenced by multiple factors. Dowman et al. (2023) reported that the concentration of bioactive compounds in Yemeni honey depends largely on honey type, floral source, environmental conditions, and processing methods, all of which shape its biological activities.

Several studies have examined Yemeni honeys. For instance, Wabaidur et al. (2020) reported total phenolic content (TPC) values ranging from 32.28 to 49.07 mg GAE/100 g in Jujube (monofloral), Cactus, and multifloral honeys, while Alzahrani et al. (2012) documented a TPC of 62.76 mg GAE/100 g in Acacia honey. The levels of phenolics, flavonoids, antioxidant activity (DPPH), and pollen-reducing power were found to be strongly influenced by botanical origin. Antioxidant activity measured by DPPH ranged between 9.16 and 66.11 mg EAQ/100 g of honey (Silva et al. 2020). Similarly, Zivkovic et al. (2019) observed radical scavenging activity in linden and forest honeys at 0.45 and 2.75 mmol Trolox equivalents/kg, respectively, concluding that darker honeys generally exhibit higher phenolic content and stronger antioxidant activity.

The antioxidant properties of honey are attributed to a diverse set of constituents, including ascorbic acid, catalase, glucose oxidase, proteins, amino acids, organic acids, flavonoids, phenolic acids, carotenoid derivatives, and melanoidins formed during the Maillard reaction. Flavonoids, particularly flavones present in honey, are known for therapeutic benefits such as anticancer and

immunosuppressive effects (Wilczynska & Zak, 2024). Bereksi-Reguig et al. (2024) further demonstrated that bioactive compound content plays a key role in antibacterial properties, with certain honeys showing promise as therapeutic alternatives.

Phenolic compounds are especially critical, as highlighted by Becerril-Sánchez et al. (2021), who emphasized their importance in biological and functional activities, linking phenolic profiles to floral source, geography, and sensory characteristics. Rehman & Majid (2020) also noted that flavonoids and polyphenols are central to honey's therapeutic value in various diseases. Moreover, phenolic acids and flavonoids serve not only as major contributors to antioxidant activity but also as natural markers of botanical origin (Sergiel et al. 2014).

Manuka honey, derived from the manuka tree (*Leptospermum scoparium*) native to New Zealand and Australia, has received considerable attention for its antioxidant properties (Alvarez-Suarez et al. 2014). Despite these findings, there remains a notable gap in the literature regarding comprehensive profiling of bioactive compounds and antioxidant activity across the wide diversity of Yemeni honey types. In particular, comparative studies between premium Yemeni honeys such as Sidr and internationally recognized antioxidant-rich honeys like Manuka are scarce. Such comparisons are essential to establish the functional and commercial potential of Yemeni honeys in both local and global markets.

Accordingly, the present study was designed with two main objectives: (1) to determine the total phenolic content (TPC), total flavonoid content (TFC), vitamin C concentration, and DPPH radical scavenging activity (IC_{50}) of five Yemeni honey types—Sorab, Acacia, Jaden, Sidr, and Maraei; and (2) to compare these parameters with those of Manuka honey.

MATERIALS AND METHODS

Study sitting

This study was conducted in Department of Biotechnology and Food Technology, Faculty of Agriculture, Thamar University, Yemen**.**

Samples collection

Yemeni honey samples were collected from different governorates as described in Table 1. and Manuka honey was purchased from Jordan. All samples were stored in dark glass containers at room temperature until they were analyzed.

Table (1) Samples of honey investigated in this study

No	Honey name	Floral origin	Region	Year	Country
1	**Jaden**	*Kleinia odora*	Raymah-Jadajid	2021	**Yemen**
2	**Sidr**	*Ziziphus spina-Christi*	Dhamar- AL-Manar Doa´ani - Hadramout	2021 2024	
3	**Acacia**	*Acacia gerardi*	Dhamar – Dawran	2021	
4	**Sorab**	*Hypoestes forskaolii*	Dhamar – Dawran	2021	
5	**Maraei** (Pasture)	Multi-flora and sugar-fed honey.	Hadramout	2021	
6	**Manuka** 263NGO (10UMF)	*Leptospermum scoparium*		2021	**New Zealand**

Manuka honey sample

Sorab plant (*Hypoestes forskaolii*).

Jaden plant (*Kleinia odora*).

Bioactive compounds and antioxidants activity determination

Total phenolic content (TPC)

The total phenolic content was determined using the Folin-Ciocalteu reagent as described by Singleton et al. (1999) with minor modification. Briefly, A 0.5 mL of honey solution (0.1 g/mL) was mixed with 2.5 mL of 0.2 N Folin-Ciocalteu reagent and incubated for 5 min. Then, 2 mL of sodium carbonate (75 g/L) was added and incubated for 2 hrs. After incubation, the absorbance was measured against methanol as blank at 760 nm using a UV-Vis spectrophotometer (Varian Cary 50, Australia). The calibration curve was constructed using gallic acid (0 - 150 µg/ml). The measurement was performed in triplicate and the total phenolic content was expressed as mg gallic acid equivalent (GAE)/100g of honey.

Total flavonoid content (TFC)

The flavonoid contents were determined using a colorimetric method adapted from Sant'ana et al. (2012). Aluminum chloride ($AlCl_3$), 2 ml were mixed with 2 ml of honey solution (500 mg/ml) and 2 ml H_2O: MeOH (1:1). The mixture was then incubated for 30 min. at 25 ˚C. The absorbance was measured at 415 nm. A calibration curve was prepared using a quercetin standard (0 – 50 µg/ml). The results were expressed as mg quercetin/100g of honey.

Vitamin C

Vitamin C (ascorbic acid) content was determined by iodine titration method with starch as indicator according to technique described by Al-Mosa et al. (2019) and Satpathy et al. (2021). In brief, 20 ml of honey solution (5 g in 100 ml distilled water) was transferred into 250 ml beaker and 1 ml of cooled, filtered starch solution (0.5%) was added. Slow titration with iodine (0.005 M) with stirring was carried out to reach the end point and dark blue color appeared. The volume of iodine used in titration was recorded and the vitamin C content was calculated as follow:

$$\text{Vitamin C (mol/l)} = \frac{\text{ml of iodine} \times \text{molarity of iodine}}{\text{Sample volume (ml)}}$$

The amount of vitamin C in (mg/100g) was calculated using the following equation: Vitamin C (mg/100g) = Vitamin C (mole/l) × M.W. of Ascorbic acid × 100.

Radical scavenging activity by DPPH assay

DPPH radical scavenging activity was measured according to Mokaya et al. (2020) with modification. Different concentrations of honey samples were prepared (0 – 25 mg/ml). One milliliter of each concentration was mixed with 4 ml of 0.1 mM methanolic DPPH solution. The tubes were shaken vigorously and incubated at room temperature for 30 min. A control was prepared using 1 ml of methanol instead of the sample and 4 ml of 0.1 mM methanolic DPPH solution. The blank consisted of 1 mL of honey solution with 4 mL of methanol. The absorbance was measured at 517 nm. The percentage of radical scavenging activity was calculated as follows: % Radical scavenging activity $= \frac{A\ control - A\ sample}{A\ control} \times 100$

Where:

A control: Absorbance of control at 517 nm,

A sample: absorbance of the sample at 517 nm.

The IC_{50} (concentration required to inhibit 50% of DPPH radicals) value for each sample was derived from the plot of % radical scavenging activity vs concentration using the linear regression equation: $\boldsymbol{y = ax + b}$, and the IC_{50} was calculated using the equation:

$$IC_{50}\ (mg/ml) = \frac{50 - b}{a}$$

Statistical analysis

All measurements were carried out in triplicate. Data analysis was performed using IBM SPSS Statistics software, version 21.0 (IBM Corp.). A one-way analysis of variance (ANOVA) was applied, followed by Duncan's HSD post-hoc test to assess multiple comparisons. Results are presented as mean values with standard deviation (SD). Statistical significance was considered at $p < 0.05$.

RESULTS AND DISCUSSION

Total phenolic contents (TPC)

The total phenolic content is widely acknowledged as a key marker of honey's antioxidant capacity, which varies considerably among different honey types due to their floral origin (Zabaiou et al. 2017; Singleton et al. 1999). Phenolic compounds are regarded as the primary contributors to antioxidant activity, and the significant variation in TPC values underscores the influence of botanical source on phenolic composition (Khalil et al. 2012). TPC content of honey samples were determinate as gallic acid equivalent (GAE) using gallic acid standard curve (Fig. 1).

As shown in Table 2, mean TPC values differed significantly ($p < 0.05$) between Yemeni and Manuka honey samples. Sidr honey exhibited the highest TPC (163.66 mg GAE/100 g), while Maraei honey recorded the lowest (33.40 mg GAE/100 g). The overall range observed in Yemeni honey (29.90–163.66 mg GAE/100g) is consistent with earlier studies. For example, Wabaidur et al. (2020) reported TPC values of 49.07, 37.46, and 32.28 mg GAE/100 g for Jujube (monofloral), Cactus, and multifloral Yemeni honeys, respectively. Likewise, Bereksi-Reguig et al. (2024) documented wide variability in TPC (24.17–122.15 mg GAE/100 g) across honey types, attributing this to differences in floral origin. Zivkovic et al. (2019) found forest honey to have the highest phenolic content (138.97 mg GAE/100 g), noting that darker honeys generally contain greater phenolic levels and stronger antioxidant activity.

The relatively low TPC in Maraei honey (33.40 mg GAE/100 g) may be linked to its production method, as this honey is often produced from bees fed sugar solutions rather than natural nectar, resulting in reduced phytochemical content. Comparable findings were reported by Silva et al. (2020), who observed phenolic contents ranging from 27.65 to 97.01 mg GAE/g, with an average of 62.66 ± 20.46 mg GAE/g across honey samples.

Table (2) Total phenolic compounds content of Yemeni and Manuka honey (mg GAE/100g)

Origin	Honey type	Mean ± SD	Min.	Max.
Yemen	Jaden	98.46 ± 4.11 ^{c}	95.00	103.00
	Sidr	163.66 ±7.26 ^{e}	155.70	169.90
	Acacia	114.66 ±7.24 ^{d}	109.90	123.00
	Sorab	67.36 ± 4.16 ^{b}	62.70	70.70
	Maraei	33.40 ± 3.36 ^{a}	29.90	36.60
New Zealand	Manuka	108.83 ± 2.51 ^{d}	106.50	111.50

Different superscript letters in column indicate statistically significant differences at ($p < 0.05$).

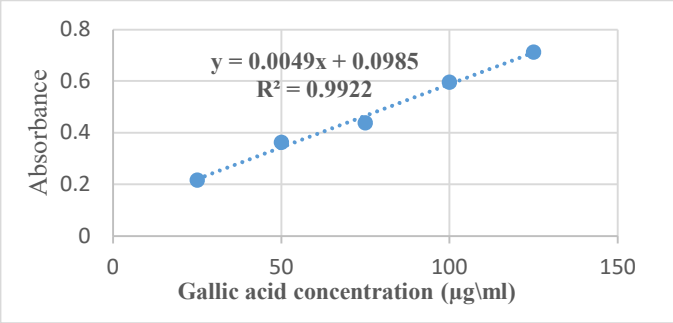

Fig. 1. Standard curve of gallic acid for total phenolic content

Manuka honey exhibited a mean TPC of 108.83, with a range (106.50 to 111.50 mg GAE/100 g), which is higher than previously reported values of 65.79 mg GAE/100g (Bundit et al. 2016) and 85.61 mg GAE/100g (Grabek-Lejko et al. 2024). Previous studies have reported the TPC of Manuka honey to be 10.399 mg GAE/100g (Joshua Boateng and Diunase, 2015), 53.5 mg GAE/100g (Kazmierczak-Baranska et al. 2024), and 89.909 mg GAE/100g (Alzahrani et al. 2012).

Notably, Yemeni Sidr and Acacia honeys exhibited higher TPC than Manuka honey, suggesting that these local honeys possess comparable or superior antioxidant potential.

Total flavonoid content (TFC)

Flavonoids are well known for their strong free radical scavenging activity and play an important role in the functional properties of honey (Beretta et al. 2005; Yao et al. 2003). TFC content of honey samples were determinate as quercetin equivalent (QE) using quercetin standard curve (Fig. 2).

Table 3 summarizes the TFC values of the analyzed honey samples. For Yemeni honeys, TFC ranged between 1.27 and 4.07 mg QE/100 g, which falls within the range (0.07–33.49 mg QE/100 g) reported by Bereksi-Reguig et al. (2024), but is markedly lower than the values (543–1302 mg QE/100 g) documented by Silva et al. (2020). Wabaidur et al. (2020) also reported relatively low TFC values for Yemeni honeys, ranging from 5.29 to 11.61 mg QE/100 g. In contrast, Manuka honey exhibited a higher TFC (6.07 mg QE/100 g) compared with Yemeni samples, consistent with its reputation for strong bioactivity.

Table (3) Total flavonoid content of Yemeni and Manuka honey (mg QE/100 g)

Origin	Honey type	Mean ± SD	Min.	Max.
Yemen	Jaden	4.07 ±0.21 ^{d}	3.90	4.30
	Sidr	2.57 ±0.21 ^{b}	2.40	2.80
	Acacia	1.27 ±0.06 ^{a}	1.20	1.30
	Sorab	3.50 ±0.10 ^{c}	3.40	3.60
	Maraei	1.63 ±0.49 ^{a}	1.30	2.20
New Zealand	Manuka	6.07 ±0.46 ^{e}	5.80	6.60

Different superscript letters in column indicate statistically significant differences at (p < 0.05).

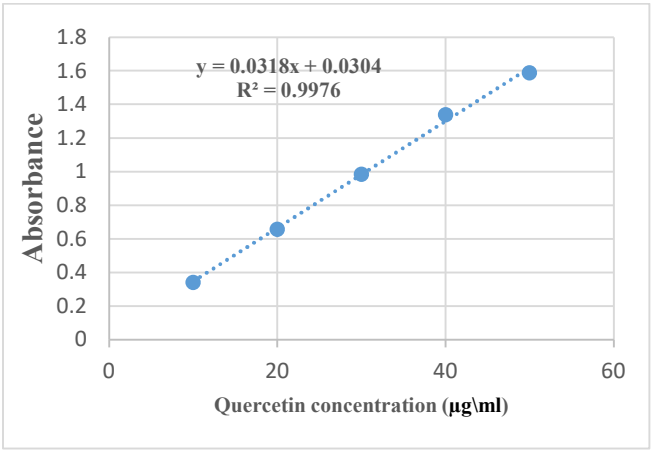

Fig. 2. Standard Curve of Quercetin (µg/ml)

TFC/TPC ratio

Flavonoid and phenolic acids are natural indicators of the botanical origin of some honeys (Sergiel et al. 2014). Fig. (3) shows the ratio of total flavonoid and total phenol content (TFC-TPC) for all honey samples tested. The values were 0.0413, 0.0153, 0.0113, 0.0520, and 0.0483 for Jaden, Sidr, Acacia, Sorab, and Maraei honey samples respectively, while it was 0.0557 for Manuka honey samples.

These results are fall in the range of (Can et al. 2015) who reported that the flavonoid expressed as quercetin equivalents represented 2-10% of the TPC of Turkish monofloral honeys, while, these results are lower than those of Zivkovic et al. (2019) who found that the lowest TFC- TPC ratio of 0.08 was in acacia honey, whereas the highest was recorded in meadow and bee pollen-enriched honey (0.13). Bueno-Costa et al. (2016) reported that honeys from several regions in Brazil possessed TFC of approximately 10% of the average total phenolic content.

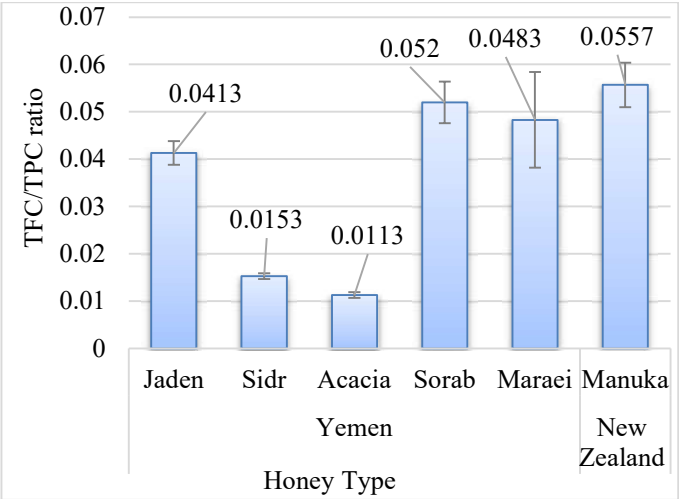

Fig. (3) TFC/TPC ratio in Yemeni and Mauka honey

Vitamin C Content

Although present in smaller quantities than phenolic compounds, vitamin C contributes significantly to the antioxidant potential of honey. Table 4 shows that vitamin C levels varied notably ($p < 0.05$) among the Yemeni and Manuka honey samples analyzed. Sidr honey contained the highest concentration (16.32 mg/100 g), while Maraei honey had the lowest (3.29 mg/100 g). Acacia and Jaden honeys also exhibited relatively high levels, at 11.42 and 9.80 mg/100 g, respectively. The reduced vitamin C content in Maraei honey may be linked to sugar-feeding practices during production rather than natural nectar collection, which limits its phytochemical richness.

Table (4) Vitamin C content of Yemeni and Manuka honey (mg/100 g)

Origin	Honey Type	Mean ±SD	Min.	Max.
Yemen	Jaden	9.8 ±0.41 ^{c}	9.45	10.25
	Sidr	16.32 ±0.73 ^{e}	15.52	16.94
	Acacia	11.42 ±0.72 ^{d}	10.94	12.25
	Sorab	6.69 ±0.42 ^{b}	6.22	7.02
	Maraei	3.29 ±0.34 ^{a}	2.94	3.61
New Zealand	Manuka	10.83 ±0.25 ^{d}	10.60	11.10

Different superscript letters in column indicate statistically significant differences at (p < 0.05).

Manuka honey contained 10.83 mg/100 g of vitamin C, which is lower than the values reported by Bundit et al. (2016), who found 106.737 mg/100 g in Manuka honey. Similarly, Al-Mosa et al. (2019) reported much higher vitamin C levels in Ziziphus and Acacia honeys (239.2 and 260.4 mg/100 g, respectively). In contrast, the Yemeni honeys analyzed in this study showed higher vitamin C content than that reported by Alwaseai et al. (2022), who found only 0.65 mg/100 g in Yemeni honey. Overall, these variations in vitamin C content highlight the strong influence of plant

source, processing conditions, and geographical region on the nutritional composition of honey (Silva et al. 2009; Alwaseai et al. 2022).

DPPH IC_{50} Scavenging activity

DPPH IC_{50} Scavenging activity of each honey sample was derived from the plot of % radical scavenging activity vs sample concentration (mg/ml) using the linear regression equation: $y = ax + b$ (Fig. 4). The antioxidant activity assessed using the DPPH assay showed no significant variation ($P<0.05$) among the honey samples analyzed (Table 5). As is well established, a lower IC_{50} value reflects stronger antioxidant capacity. Manuka honey demonstrated the highest radical scavenging activity, with the lowest IC_{50} value (11.07 mg/ml). Among the Yemeni honeys, Sidr honey exhibited the strongest activity (IC_{50} = 30.84 mg/ml), while Jaden honey showed the weakest (IC_{50} = 42.13 mg/ml).

These results are in line with previous reports. Alzahrani et al. (2012) documented IC_{50} values of 13.46 mg/ml for Manuka honey and 13.62 mg/ml for Acacia honey. Similarly, Bereksi-Reguig et al. (2024) reported a broad range of IC_{50} values (22.91–98.58 mg/ml) across different honey types. The comparatively lower antioxidant activity of Yemeni honeys relative to Manuka may be attributed to differences in floral sources and phenolic composition.

According to Sakika et al. (2022), honey samples with IC_{50} values between 10 and 50 mg/ml are classified as having strong antioxidant activity, those between 50 and 100 mg/ml as intermediate, and values above 100 mg/ml as weak. Based on this classification, all Yemeni honey samples in the present study fall within the strong antioxidant activity category.

Table (5) DPPH IC_{50} scavenging activity of Yemeni and Manuka honey (mg/ml)

Origin	Honey type	Mean ± SD	Min.	Max.
Yemen	Jaden	42.13 ±6.55 [b]	37.61	49.64
	Sidr	30.84 ±5.90 [ab]	25.88	37.37
	Acacia	32.68 ±6.03 [ab]	25.88	37.38
	Sorab	37.89 ±28.02 [ab]	21.71	70.24
	Maraei	36.34 ±16.0 [ab]	21.38	53.22
New Zealand	Manuka	11.07 ±0.53 [a]	10.52	11.57

Different superscript letters in column indicate statistically significant differences at ($p < 0.05$).

Importantly, the DPPH IC_{50} of Sidr honey (30.84 mg/ml) was within the range of values reported for many commercial honeys with acknowledged bioactivity. This finding supports the traditional use of Yemeni Sidr honey as a health-promoting product.

The results demonstrated variations in the antioxidant activity among the honey samples. These variations reflect differences in botanical origin and highlight the diverse quality attributes of the honey samples.

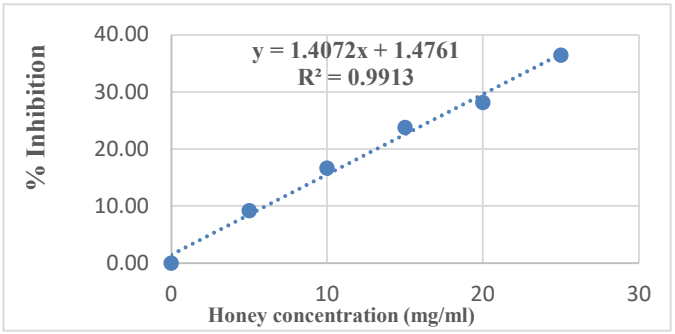

Fig. (4) DPPH scavenging activity curve of honey sample (mg/ml)

CONCLUSIONS

This study demonstrates that Yemeni honeys, particularly Sidr and Acacia honeys, contain substantial amounts of TPC and vitamin C, which contribute to their antioxidant activity. Yemeni Sidr and Acacia honey contains TPC and vitamin C amount higher than Manuka honey, supporting its value as a bioactive natural product. Significant variations in bioactive compound content among Yemeni honey samples highlight the influence of geographical origins and botanical source. Future studies should include more Yemeni honey types using modern techniques such as HPLC-based profiling of individual phenolic compounds.

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AUTHOR CONTRIBUTIONS

HHA Al-Khawlani, AM Alwaseai, MM Alsharhi authors equally contributed on protocol proposal, collection, processing, analyzed, interpretation of data and wrote first & final version of Manuscript. All Authors have approved this version of the manuscript.

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CONFLICT OF INTEREST

The authors have declared no conflict of interest.

ETHICAL STANDARDS

The study received approval from the Faculty of Agriculture, Thamar University.

DATA AVAILABILITY:

All data generated and analysed during this study are included in this published article.

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الفينولات الكلية والفلافونيدات والفعالية المضادة للأكسدة في أنواع من العسل اليمني مقارنةً بعسل المانوكا

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الملخص

هدفت الدراسة الى تقدير الفينولات الكلية والفلافونيدات وفيتامين C والفعالية المضادة للأكسدة مقدرة في صورة DPPH IC_{50} في أنواع من العسل اليمني ومقارنتها بعسل المانوكا. شملت الدراسة خمسة أنواع من العسل اليمني: (عسل احادي الزهرة) صورب واكاسيا من محافظة ذمار وجعدن من محافظة ريمة وسدر من محافظتي ذمار وحضرموت) و(عسل متعدد الزهرة) مراعي من محافظة حضرموت ونوع واحد من عسل (المانوكا من نيوزيلاندا). تم تقدير كلاً من الفينولات الكلية والفلافونيدات وفيتامين C والفعالية المضادة للأكسدة DPPH IC_{50} في عينات العسل. أظهرت النتائج ان الفينولات الكلية كانت تتراوح ما بين 33.40 الى 163.66 (مليجرام 100/GAE جرام)، والفلافونيدات الكلية كانت ما بين (1.27 الى 4.07 مليجرام 100/QE جرام) وفيتامين C ما بين (3.29 الى 16.32 مليجرام/100 جرام)، والفعالية المضادة للأكسدة DPPH IC_{50} (30.84 الى 42.13 مليجرام/مل) في العسل اليمني، في حين كانت الفينولات الكلية (108.83 مليجرام 100/GAE جرام) والفلافونيدات الكلية (6.07 مليجرام 100/QE جرام)، وفيتامين C (10.83 مليجرام/100 جرام)، والفعالية المضادة للأكسدة DPPH IC_{50} (11.07 مليجرام/مل) في عسل المانوكا. كما أظهرت النتائج ان عسل السدر اليمني كان يحتوي على اعلى نسبة من الفينولات الكلية وفيتامين C حيث بلغت (163.66 ± 7.26 مليجرام 100/GAE جرام) و (16.32 ± 0.73 مليجرام/100 جرام) على التوالي مقارنةً بكافة عينات العسل التي شملتها الدراسة، في حين حقق عسل المانوكا اعلى فعالية مضادة للأكسدة (أقل قيمة لـ IC_{50} = 11.07 مليجرام/مل)، كذلك كان لعسل السدر اليمني فعالية مضادة للأكسدة مقاربة للفعالية لعسل المانوكا مما يؤكد قيمته العالية كمنتج ذات فعالية حيوية عالية.

الكلمات المفتاحية: مضادات الاكسدة، العسل اليمني، DPPH IC_{50}، فيتامين C، الفينولات الكلية، الفلافونيدات، عسل المانوكا.

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Full length article

Factors affecting weight at first service of Holstein Friesian heifers born and reared in a tropical environment

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ABSTRACT

The introduction of Holstein Friesian to an environment out of their thermo-comfort zone and to diseases not existing in their original temperate climates, was assumed to affect their reproductive and productive performance. From this assumption came the need to investigate and evaluate the performance of this breed in the hot climate of Northern Sudan, hence the objective of this study. The trait studied was weight at first service under the factors of year and season of birth of heifer, weaning weight class, weaning age class and their interactions. The method of data analysis was the Least Mean Squares. The data were subjected to analysis of variance using the SPSS program version 12.5. A total number of 588 records covering the period from the year 1989 to the year 2002 were retrospectively collected and analyzed. The results showed that the overall mean weight at first service was 337.25 ± 2.76 kg. The effect of the year of birth of heifers on this trait was highly significant (P≤ 0.001). The season of birth of the heifers, age at weaning and weight at weaning exerted no significant effects on the weight of heifers at first service (p ≥ 0.05). The interactions of these factors also showed no significant effect on the trait (p≥ 0.05). The weight at first service revealed by this study was not far from the breed norms in their countries of origin. We can conclude that the Holstein Friesian heifers born and reared under the prevailing environmental and management conditions at the farm of study were able to adapt and perform satisfactorily.

Keywords: First service, Holstein Friesian, Tropical environment, Weight

INTRODUCTION

The Holstein Friesian breed of cattle originated in the northern regions of Holland and Germany. Its name is derived from the Friesland province in Holland and the Holstein province in northern Germany, where the breed was historically concentrated. Renowned as the world's highest milk-producing cattle, Holstein Friesians have spread far beyond Europe and are now widely raised in dairy farms across the world (Anonymous, 2026).

Adult Holstein Friesian cows typically weigh between 690–770 kg and stand 140–165 cm tall. At birth, healthy calves weigh around 40–50 kg. By 14 months of age, when they reach an average weight of 320 kg, they are ready for breeding. Farmers generally plan for heifers to calve for the first time at about 22 months, when they have attained roughly 80% of their mature body weight (Anonymous, 2026).

Although often overlooked in dairy operations, raising heifers is crucial since they represent the future

of the herd. In some countries, commercial production systems that employ advanced technologies in milk production and animal husbandry account for about 10% of total output, particularly where exotic dairy breeds are kept (Hammoud et al., 2010).

Reproductive performance in dairy cows is influenced by multiple factors, including breed, calving, season, environment, and management practices. Key indicators of productive efficiency include milk yield and days in milk, while reproductive indices encompass age at first calving, days open, services per conception, and calving interval (Tadesse, 2010; Amene et al., 2011; Usman et al., 2013; Hoka et al., 2019).

Regular monitoring of body weight (BW) and growth rate provides valuable insights for farmers, enabling better decision-making. Tracking BW in future dairy cows enhances herd productivity and reduces disease incidence (Costa et al., 2021). Genetic and environmental factors—such as calving weight, nutrition, litter size, gestation length, calving year, season, insemination bull, calf gender, type of birth, geographical region, and altitude—can all affect the weight of heifers or cows at first service (Yaylak et al., 2015).

Live weight is considered the most critical factor influencing puberty (Ugarte, 1989). Large breeds typically reach puberty at around 270 kg, while smaller breeds do so at approximately 240 kg. It is therefore more effective to use target live weights rather than age when planning heifer mating. In tropical regions, recommended breeding weights are 200–220 kg for smaller breeds and 290–310 kg for larger breeds (Moran, 2012).

This study was designed to evaluate the impact of year and season of birth, age, and weaning weight on the body weight of Holstein Friesian heifers at first service, under the prevailing farm management practices and tropical environmental conditions of Northern Sudan.

MATERIALS AND METHODS

Farm Location and Establishment

The farm under study belonged to the Arab Company for Agricultural Production and Processing (ACAPP). This company was one of the largest companies established by the Arab Authority for Agricultural Investment and Development (AAAID). This farm is located about 40 Km south of khartoum at Al Bagair area .It lies about 4Km West of khartoum –Medani road .It was established in 1984 ,it started by importing 1000 heifer-in-calf in two batches (500 heads each)in 1984 and 1985 from West Germany .They were pedigree registered Holstein –Friesian heifers.

Environmental Conditions in the farm Area:

Meteorological data showed that the average annual rainfall in the farm area was 167mm.There was a wet season from July to September with 70% of the total annual rainfall falling within this period. Temperatures in the area were high with an annual mean average of 30.7°C, and extremes of over 45°C. The hotter months were June and July with a mean average of about 35.5 °C. The lowest temperatures were recorded in January with a mean average of 24.6 °C. Relative humidity recorded at 6: 00 GMT was 13% and was 40% at 12: 00 GMT. It was 52% at 18: OO GMT. Relative humidity was lowest in March and April and highest in August. The mean wind speed varied between 3.10 m./sec. In October and 4.40 m./sec. in several months during the year.

The Management System in the Farm

Housing

Each 500 cows were kept in a cow sub-unit. The sub-unit comprised a single steel-frame building of 6900 m2. The building contained 10 cow pens, milking parlour, holding areas and storage and cooling facilities. The building was essentially open with the southern side being provided with low walls and shutters to give protection from dust storms. Adequate ventilation was ensured through the open gables and an open ridge. Each group of 48 cows was having a shaded resting and feeding area of 7.7 m2 per cow and free access to an open exercise yard of 4.3o m2/cow. Free access to drinking water was ensured in the shaded area the floor of the covered and open areas was concrete.

The Feeding System

The animals were fed on green or dry roughage (mainly sorghum hybrid) and a concentrate mix. The concentrate mix generally consisted of oil seed cakes, wheat bran, sorghum grain, molasses, sorghum gluten, salts and lime. There were fluctuations in the quantity and quality of both roughage and concentrate rations from year to year and from season to season. The roughage was offered once a day while the concentrate mix was given twice daily after milking.

Milking Practice

Machine milking was adopted in the farm. Each 500 cow sub-unit was supplied with a- 16 x 2(units) milking parlour with milk storage and cooling facilities. Cows were milked twice daily as a routine, but in some years, when good levels of nutrition were secured, three-times –milking per day was practiced.

The Breeding Program

Artificial insemination (A.I.) was the main method adopted for breeding females in the farm. High quality frozen semen from proven Holstein-Friesian sires was imported every year. Cows that return to A.I. were referred to natural service by a bull from the herd. The farm kept pure Holstein-Friesian animals since its

establishment. Neither cross-bred animals were introduced nor cross-breeding was practiced in the farm.

Animal Health and Disease Control

Vaccination against the major prevailing epidemic diseases in the Sudan was a regular practice in the farm. The main diseases vaccinated against were Rinderpest, Anthrax, Black Quarter, Hemorrhagic Septicemia, Contagious Bovine Bleuro-pneumonia and Foot and Mouth Disease. Female calves at the age of four to eight months were vaccinated against Brucellosis using stain 19. Cows were vaccinated against Brucellosis using K 49/vaccine and diluted strain 19. Tick control was practiced by regular spraying of all animals with acaricides Spraying was done once – weekly in the first year of importing the animals, then twice-monthly afterwards.

Source and collection of data

This study was conducted retrospectively using 558 Holstein Friesian heifers' records for documenting their weight at first service and associated factors under the prevailing farm management practices and tropical environmental conditions from 1989 to 2002 at the Arab Company for Agricultural Production and Processing (ACAPP), Northern Sudan.

Statistical analysis:

The data were analyzed by the method of Least Mean Squares (Steel, Torrie and Dickey, 1997). They were subjected to analysis of variance using SPSS program version 12.5.
Fixed model:

$$Yijkl=\mu+Yi+Sj+AWK+WWI+(Y\times S)+(Y\times AW)+(Y\times WW)+(S\times AW)(S\times WW)+ E ijKL$$

Where:
Yijkl = The trait studied
μ = Overall mean
Yi= effect of year of birth
Sj= effect of Season of birth
AWK= effect of Class of Age at Weaning
WWI= effect of Class of Weight at Weaning
(Y×S),(Y×AW),(Y×WW),(S×AW), (S×WW)= interactions
Eijkl = Standard error.

RESULTS &DISCUSSION

The trait was examined under the factors of year and season of birth, weaning weight class, weaning age class, and their interactions. Statistical analysis revealed that the overall mean body weight at first service for Holstein-Friesian heifers at the study farm was 337.25 ± 2.76 kg (Table 1). These findings are consistent with those reported by Roger et al. (1983), Muller and Botha (2000), Archbold et al. (2012), and Cook (2019). Conversely, they differ from the results presented by Ugrate (1989), Menjo et al. (2009), Duplessis et al. (2015), Bazely et al. (2016), Le Cozler (2019), and Levina et al. (2019). Such discrepancies in body weight may be attributed to evolving standards over time or variations in management practices, including feeding strategies, housing systems, and record-keeping methods, as previously highlighted by Heinrichs and Losinger (1998).

Table 1: Overall mean ± standard Error of heifer's weight (Kg) at first service

Breed	No. of Records	Mean (Kg)	Std. Error
Holstein Friesian	558	337.25	2.76

Table 2: Analysis of variance for the effect of year & season of birth, class of age at weaning, class of weight at weaning & their interactions on weight at first service of heifers

Source of Variation	df	Mean Square	F	Sig.
Years of birth	6	24018.06	13.97	0.00
Season of birth	2	31.09	0.18	0.83
Class of Age at Weaning	3	751.59	0.44	0.74
Class of Weight at Weaning	2	1716.79	1.00	0.37
Years of birth * Seasons of birth	11	1119.56	0.65	0.78
Years of birth * Class of Age at Weaning	14	1098.26	0.64	0.83
Season of birth * Class of Age at Weaning	6	594.96	0.35	0.91
Years of birth * Class of Weight at Weaning	10	634.18	0.37	0.96
Season of birth * Class of Weight at Weaning	4	553.80	0.32	0.86
Class of Age at Weaning * Class of Wt. Weaning	6	2115.68	1.23	0.29

In this study, the year of birth of the heifer had a highly significant effect on body weight at first service ($P < 0.001$) (Table 2). As shown in Table 3, the highest mean weight at first service (375.88 ± 2.76 kg) was recorded during the 1993–1994 period, while the lowest mean weight (288.36 ± 7.70 kg) occurred in 1997–1998. This substantial variation is likely linked to the severe resource shortages the farm experienced in certain years of operation.

Table 3: Means ± standard Errors of weight (Kg) at first service in the different years of birth of heifers.

Years of Birth	Mean (Kg)	Std. Error
1989-1990	325.93	10.37
1991-1992	331.44	5.11
1993-1994	375.88	4.80
1995-1996	299.42	11.49
1997-1998	288.36	7.70
1999-2000	358.21	7.07
2001-2002	360.00	13.33

The influence of environmental factors on heifer body weight across different seasons is presented in Table 4. As shown, heifers born during winter exhibited higher mean body weights (339.11 kg), whereas those born in the dry summer recorded lower weights (333.47 ± 5.19 kg) as presented in Table 4. Statistically, however, the season of birth did not have a significant effect on weight at first service ($p \geq 0.05$), as indicated in Table 2. These findings are consistent with the results of Singh and Gurnani (2002), Elabdein and Makkawi (2006), and Hurst (2021), but differ from those reported by Singh and Gurnani (2002), Uhrincet et al. (2021), and Hurst et al. (2021). The observed variation in mean heifer weight across seasons may be explained by the observations of Fedorovych et al. (2023), who emphasized that seasonal climatic changes and fluctuations in feed availability significantly affect animal growth and are increasingly important considerations in breeding strategies.

Table 4: Means and standard errors of weight (Kg) at first service in the different seasons of birth of heifers

Season of Birth	Mean (Kg)	Std. Error
Winter (Nov.- Feb.)	339.11	4.53
Dry Summer (March – June)	333.74	5.19
Wet Summer (July – Oct.)	338.53	4.66

In this study, the effect of weaning weight on weight at first service was found to be non-significant ($p \geq 0.05$), as shown in Table 5. However, heifer calves weaned at body weights greater than 70 kg tended to reach first service at a higher weight (345.85 kg), as indicated in Table 5. This trend was likely influenced by management practices, particularly nutrition. These findings are consistent with those of Machado et al. (2025), who reported a very weak association between body weight and fertility in heifers. In contrast, Ugrate (1989), Gaafar et al. (2005), documented different outcomes, suggesting that weaning weight did affect weight at first service. Such discrepancies among studies may be attributed to the fact that weaning is a management decision, shaped by the specific conditions prevailing on each farm.

Table 5: Means and standard errors of weight (Kg) at first service at different classes of weight at weaning

Class of Weight at Weaning (Kg)	Mean	Std. Error
40 – 55	335.88	5.39
56 -70	329.21	4.42
> 70	345.85	4.65

Analysis of the effect of age at weaning on body weight at first service revealed no significant differences ($P \geq 0.05$), as shown in Tables 2 & 6. The variations among age classes in relation to weight at first service were relatively minor, likely reflecting management decisions and practices. In contrast, Costigan et al. (2022) and Constantin (2023) reported that age at weaning did have an impact on heifer weight at first service. These discrepancies may be attributed to differences in farm-specific weaning policies, which are often tailored to individual management conditions and resource availability.

Table 6. Means and standard errors of weight (Kg) at first service at different classes of age at weaning of heifers

Class of Age at Weaning (Days)	Mean	Std. Error
42 – 60	342.34	6.75
61 – 75	333.04	3.99
76 -90	340.28	5.65
> 90	336.78	6.99

CONCLUSION

The findings of this study reveal that heifers born and raised in the hot climate of the Northern Gezira were able to achieve body weights at first service comparable to those reported in countries with temperate or similar environments, despite the challenging conditions. This highlights their ability to adapt to prevailing environmental stresses. Moreover, these results provide valuable guidance for farm management practices and support recommendations concerning the introduction and effective management of temperate dairy breeds in Sudan.

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Author contributions

Ismail Mohamed Elfagir, Abdelmoniem M. Abu Nikhaila, Tarig A. A., Mohamed Khair Abdallah, and Adil Mousa Younis Waniss, the 5 authors equally contributed on proposal plan, Data collection, processing, analyzed, interpretation of data, wrote first & final draft of Manuscript. All Authors have approved this version of the manuscript.

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Conflict of interest

The authors have declared no conflict of interest.

Ethical standards

The Faculty of Animal Production, University of Khartoum, Sudan, approved the study.

Data availability

All data generated and analyzed during this study are included in this published article.

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العوامل المؤثرة على وزن عجلات الهولشتاين فريزيان عند أول تلقيح لها والمولودة والمرباة في البيئة الاستوائية

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الملخص

ان إدخال أبقار الهولشتاين فريزيان إلى بيئة خارج نطاق بيئتها، وعرْضها لأمراض غير موجودة في مناخاتها المعتدلة الأصلية، افترض أنه سيؤثر على أدائها الإنتاجي والتناسلي. ومن هذا الافتراض جاءت الحاجة إلى دراسة وتقييم أداء هذا السلالة في المناخ الحار لشمال السودان، كانت الصفة المدروسة في هذه الدراسة الاستعادية هي وزن العجلات عند أول تلقيح لها، والعوامل المؤثرة عليها مثل سنة وموسم الميلاد، وفئة وزن الفطام، وفئة عمر الفطام. تم استخدام طريقة المتوسطات المربعة الصغرى لتحليل البيانات، وأُخضعت البيانات لتحليل التباين باستخدام برنامج SPSS .تم جمع وتحليل ما مجموعه 588 سجلاً تغطي الفترة من عام 1989 إلى عام 2002. أظهرت النتائج أن متوسط الوزن للعجلات عند أول تلقيح كان 2.76± 337.25 كجم. كشف التحليل الاحصائي ان سنة الميلاد كان لها تأثير معنوي ذو دلالة إحصائية (P≤0.001)على وزن العجلات عند اول تلقيح، بينما لم يكن لموسم الميلاد، أو عمر الفطام، أو وزن الفطام أي تأثير معنوي. كما ان كشفت نتائج هذه الدراسة أيضا ان وزن العجلات عند أول تلقيح لم يكن بعيداً عن القياسات والصفات الخاصة بالسلالة في بلدانها الأصلية. خلصت الدراسة الى ان عجلات الهولشتاين فريزيان المولودة والمرباة في مزرعة الهيئة العربية للاستثمار والانماء الزراعي كانت قادرة على التكيف والأداء بشكل مرضٍ تحت الظروف البيئية والإدارية السائدة في منطقة الدراسة.

الكلمات المفتاحية: أول تلقيح، الهولشتاين فريزيان، البيئة الاستوائية، الوزن

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Full length article

Streptococcus pyogenes in human at Dhamar, Yemen: Prevalence and antimicrobial susceptibility profiles

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ABSTRACT

This cross-sectional study was carried out across multiple areas of Dhamar, Dhamar Governorate between 2024 and 2025 to assess the prevalence of *Streptococcus pyogenes* among individuals and to evaluate the antimicrobial susceptibility of the isolated strains. A total of 381 throat swabs were collected from participants presenting with sore throat of varying severity. Samples were transported to the Faculty of Veterinary Medicine, Thamar University, where culture and biochemical analyses were performed. Out of the 381 samples examined, 67 (17.59%) tested positive for *S. pyogenes*. The highest prevalence was observed in Robbat Al-Qalah (4.72%), while the lowest was recorded in Rakhamah (0.26%). Age-wise distribution showed the highest prevalence in the 5–15 years group (7.61%), and the lowest in individuals aged 45 years and above (2.36%). Seasonal variation revealed the peak prevalence in October (4.99%) and the lowest in March (0.79%). Statistically significant differences ($P < 0.05$) were noted in prevalence across locations and months. Antimicrobial susceptibility testing indicated that the isolates were sensitive to Penicillin G, Amoxicillin, Ampicillin, Cefotaxime, Cephalosporins, Ceftriaxone, Lincomycin, and Vancomycin. Conversely, resistance was observed against Streptomycin, Gentamicin, Levofloxacin, Tetracycline, Erythromycin, and Clindamycin. In conclusion, *Streptococcus pyogenes* is prevalent in the studied areas of Dhamar Governorate. Routine monitoring of antibiotic resistance in both human and veterinary contexts is recommended. Further epidemiological investigations are warranted to expand knowledge of streptococcal infections in other regions of the governorate.

Keywords: *Streptococcus pyogenes*, Antimicrobial Resistance, Dhamar, Yemen.

INTRODUCTION

Streptococci are Gram-positive bacteria that typically occur in chains or pairs. They form part of the normal flora of humans and animals, yet several species act as pathogens. The most significant among them is *Streptococcus pyogenes*, the primary cause of pyogenic infections (Kushwaha et al., 2014). Classified under Lancefield Group A, this beta-hemolytic species is commonly referred to as Group A beta-hemolytic Streptococci (GABHS). Group A Streptococcus (GAS) consists solely of *S. pyogenes* (Khan et al., 2002). Food, milk, and dairy products can serve as vehicles for transmitting this organism to humans and animals (Jakee et al., 2013; Rifa et al., 2025).

Although *S. pyogenes* can infect individuals of all ages, children are particularly susceptible (DeMuri & Wald, 2014). It is capable of producing a wide spectrum of diseases, ranging from mild conditions such as pharyngitis and impetigo to life-threatening illnesses including streptococcal toxic shock syndrome, necrotizing fasciitis, acute rheumatic fever, and acute glomerulonephritis (Carapetis et al., 2005; Luca-Harari et al., 2009; AlShamisi, 2016; Pickering et al., 2025). Mortality rates from severe

GAS infections remain high worldwide, affecting both developed and developing nations (Steer et al., 2007; Lepoutre et al., 2011).

The prevalence of *S. pyogenes* infections reflects the interaction of three key factors: the pathogen itself, host immunity, and environmental influences (Verma et al., 2018; Biała et al., 2025). Globally, the bacterium is responsible for approximately 616 million cases of pharyngitis and 111 million cases of pyoderma in children each year (Sanyahumbi et al., 2016). Severe GAS diseases affect around 18 million people, with 1.78 million new cases and at least 517,000 deaths annually, most occurring in low-income regions (Tesfaw et al., 2015; Barth et al., 2020; Gashaw et al., 2025).

Culture techniques and subsequent bacteriological procedures remain the gold standard for diagnosing GAS infections (Saleh, 2009; Hassanain et al., 2024). Penicillin continues to be the most widely prescribed treatment for acute streptococcal infections such as pharyngitis and tonsillitis. However, indiscriminate antibiotic use without medical supervision contributes to the emergence of resistant strains and promotes carrier states (Devi et al., 2011; Dunne et al., 2013).

Despite the substantial burden of GAS on human and animal health and its serious public health implications, limited research has been conducted on its epidemiology and antimicrobial resistance. This study therefore aims to assess the prevalence and antimicrobial susceptibility patterns of GAS among individuals in Dhamar Governorate, Yemen.

MATERIALS AND METHODS

Study area

This cross-sectional study was conducted between March 2024 and October 2025 across several areas of Dhamar, Dhamar Governorate. Geographically, Dhamar is situated at 14°33′0″N and 44°24′6″E, at an elevation of approximately 2,400 meters above sea level. The region experiences average summer temperatures of around 28.2 °C, while in winter, nighttime and early morning temperatures often fall below zero. The average relative humidity is 49%. Dhamar Governorate has a population of about 1,668,167 and covers an area of 7,587 square kilometers, representing a significant portion of the country's total land area.

Study population

The study population were from different areas of Dhamar. Eligible participants for entry into the study were those living in Dhamar, aged 5–46 years with history of sore throat and evidence fever. Patients who had used antibiotics in the 2-week period prior to this current illness were excluded. The sample size was calculated by the statistical program of Epi-info (version 6.04). The required sample size **is** 381 participants.

Collection of Samples

Throat swab samples were collected following the procedures described by El-Ghany et al. (2015), Spellerberg & Brandt (2022), and Kumsal et al. (2023). In brief, the sampling process was explained to each participant prior to collection. Under adequate lighting, participants were asked to open their mouths as widely as possible. Using a tongue depressor, the investigator gently rubbed a sterile cotton swab over the tonsillar area, avoiding contact with the tongue and lips to minimize contamination by oral microbiota.

The collected swabs were immediately placed in aseptic containers, labeled, and transported to the Microbiology Laboratory at the Faculty of Veterinary Medicine, Thamar University, Dhamar. Samples were obtained from several areas of Dhamar, Dhamar Governorate, including Dhamar city, Thi Sahar, Al-Melaah, Al-Moaheb, Dhamar Al-Gharn, Manghathah, Rakhamah, and Robbat Al-Qalah. Additional information such as participant age, location, and month of collection was also recorded. All samples were delivered to the laboratory within one to two hours of collection for processing.

Processing of samples

Culture, Isolation and Identification

In the laboratory, each swab was first rolled over a small portion of a sheep blood agar plate. The inoculum was then streaked across the remainder of the plate using a sterile loop to obtain well-isolated colonies, followed by incubation under anaerobic conditions at 37 °C for 24 hours. After incubation, small grayish-white colonies surrounded by clear zones of hemolysis were selected and subjected to Gram staining and the catalase test. Colonies that appeared in chains and tested catalase-negative were sub-cultured on 10% sheep blood agar containing a low concentration of bacitracin and incubated again at 37 °C for 24 hours.

Streptococcus pyogenes was identified based on sensitivity to bacitracin and confirmed using a Rapid Antigen Detection Test (RADT). All procedures were performed according to the methods described by Cheesbrough (2006), Ba-Saddik et al. (2014), Ashgar et al. (2017), Spellerberg & Brandt (2022), and in line with the manufacturer's instructions.

Antibacterial susceptibility

All isolates were subjected to *in vitro* antibiotic drug susceptibility test as per method described by Cheesbrough (2006) and Ranjan et al. (2010). The antimicrobials commercially available in 'market used for treatment of Streotococci infections such as Penicillin G, Amoxicillin, Gentamicin, Tetracycline, Ampicillin, Streptomycin, Cephalosporin, Erythromycin, Lincomycin,

Vancomycin, Clindamycin, Levofloxacin, Cefotaxime and Ceftriaxone were tested *in vitro* for their efficacy against various isolates identified in this study. The antimicrobial discs were placed on the surface of an agar plate previously seeded with a standard amount of the organism to be tested. The plates were incubated at 37°C for 18-24 hours subsequently; the plates were examined for the development of zone of inhibition around the discs. The diameter of the zone of inhibition was measured in mm and compared with the values listed in standard chart provided by the manufacturer, on the basis of which the isolates were categorized as resistant (R), moderately sensitive (M) or highly sensitive (S) to the antimicrobial contained in that particular disc.

Statistical of analysis

The collected raw data were organized using Microsoft Excel spreadsheets and analyzed with SPSS statistical software, version 20. Descriptive statistics were applied to calculate prevalence percentages. Chi-square tests were performed to assess associations between *Streptococcus pyogenes* prevalence and potential risk factors, including age, month of collection, and geographic area. Statistical significance was determined at a threshold of **P < 0.05.**

RESULTS

Prevalence of *Streptococcus pyogenes*

The results of isolation and identification of *Streptococcus pyogenes* and it`s prevalence in participants is presented in Table 1. As shown, out of 381 throat swab samples examined, 67(17.59%) were found positive for *S. pyogenes.*

Table 1. Overall Prevalence of *Streptococcus pyogenes* in participants at Dhamar Governorate

No. of Samples examined	No. of Positive samples	Prevalence %
381	67	17.59

The distribution of *S. pyogenes* according to source of samples /study areas are depicted in Table 2. As shown, the highest prevalence rate was recorded in Robbat AlQalah area (4.72%); whereas, the lower rate in Rakhamah (0.26 %). Statistically, significant differences (P<0.05) were observed between prevalence and study area.

The distributions of *S. pyogenes* according to age are presented in Table 3. As shown, the higher prevalence rate was recorded in age group of 5-15 years old (7.61%); whereas the lower rate in age group of 36-46 years old (2.36%). The age factor did not influence(P<0.05) on the prevalence rate distribution among the participants.

Table 2. Prevalence of *Streptococcus pyogenes* in participants according to study area (n=381)

Area	No. of Positive samples	Prevalence %	*P* Value
Dhamar city/district	4.0	1.05	**0.008**
Thi Sahar	3.0	0.79	
Al-Melaah	9.0	2.36	
Al Moaheb	12	3.15	
Dhamar Algharn	13	3.41	
Manghathah	7.0	1.84	
Rakhamah	1.0	0.26	
Robbat AlQalah	18	4.72	
Total	67	17.59	

Table 3. Distribution of *Streptococcus pyogenes* in participants according to ages (n=381)

Age group	No. of Positive samples	Prevalence %	*P* Value
5-15 Yrs	29	7.61	0.309
16-20 Yrs	18	4.72	
21-35 Yrs	11	2.89	
36-46 Yrs	9	2.36	
Total	67	17.59	

Considering the distribution of *S. pyogenes* according to Month-wise, the results are presented in Table 4. As shown, the higher prevalence rate was recorded in month of October (4.99%) whereas, the lower rate recorded in month of March (0.79 %). Statistically, significant differences (P<0.05) were observed between prevalence rates of *S. pyogenes* and months factor.

Table 4. Distribution of *Streptococcus pyogenes* in participants according to month variation(n=381)

Month	No. of Positive samples	Prevalence %	P value
Mar	3.0	0.79	0.031
Apr	6.0	1.57	
May	8.0	2.10	
Jun	10	2.62	
Jul	9.0	2.36	
Aug	7.0	1.84	
Sep	5.0	1.31	
Oct	19	4.99	
Total	67	17.59	

Susceptibility of isolates to antibacterial drugs

The susceptibility of isolates to antibacterial agents was evaluated in this study. The findings showed that *S. pyogenes* was sensitive to most of the tested antibacterial, including Penicillin G, Amoxicillin,

Ampicillin, Cefotaxime, Cephalosporins, Ceftriaxone, Lincamycin, and Vancomycin. In contrast, resistance was observed against Streptomycin, Gentamycin, Levofloxacin, Tetracycline, Erythromycin, and Clindamycin. For the remaining antibacterial agents tested, the isolates exhibited either intermediate resistance or complete resistance (see Table 5).

Table 5. Susceptibility patterns of S. *pyogenes* isolates to antimicrobial drugs (n=67)

Antibacterial	No. of isolates	Susceptibility
Penicillin G	67	S
Amoxicillin	67	S
Ampicillin	67	S
Tetracycline	67	R
Cephalosporin	67	S
Erythromyin	67	R
Gentamycin	67	R
Streptomycin	67	R
Levofloxacin	67	R
Ceftriaxone	67	S
Cefotaxime	67	S
Lincamycin	67	S
Clindamycin	67	R
Vancomycin	67	S

S= Sensitive, R= Resistant

DISCUSSION

Prevalence of *Streptococcus pyogenes*

The present study was conducted to identify and determine the prevalence of *Streptococcus pyogenes* and to assess the antibiogram of isolates collected from Dhamar, Dhamar Governorate. Examination of throat swab samples revealed an overall prevalence rate of 17.59%. These findings are consistent with those reported by Shulman et al. (2012), Olivieri et al. (2015), Biała et al. (2025), Šlosárková et al. (2019), and Khalaf et al. (2020), who documented prevalence rates of 12.4%, 14.3%, 16%, 17.9%, and 20%, respectively. However, the prevalence observed in this study was higher than that reported by Belachew (2016), Li et al. (2018), Verma et al. (2018), and Pickering et al. (2025), who recorded rates ranging between 5.5% and 7%. Variations in prevalence rates between studies may be attributed to differences in sample size, diagnostic techniques, and the availability of healthcare services. Moreover, since *S. pyogenes* commonly inhabits the upper respiratory tract and other organs of the human body, its frequent detection at relatively high rates is expected.

Geographical differences were also noted. The highest prevalence was recorded in Robbat Al-Qalah, while the lowest was observed in Rakhamah. These variations may be linked to environmental conditions and disparities in access to medical facilities. Additionally, clinical cases of sore throat were more frequently reported in Robbat Al-Qalah, likely due to poor housing, inadequate drainage systems, and insufficient personal and environmental hygiene in that area.

Age was found to play a significant role in the distribution of *S. pyogenes*. The highest prevalence was observed among individuals aged 5–15 years, whereas the lowest was recorded in those aged 45 years and above. These results align with the findings of Vijaya et al. (2013), Othman et al. (2019), Frenck et al. (2023), and Tyrrell et al. (2024), who noted that streptococcal infections tend to decline with increasing age. The higher prevalence in younger age groups may be explained by immunological factors.

Seasonal variation was also evident. The highest prevalence was recorded in October, while the lowest occurred in March. These results are consistent with those of Saleh (2009), who reported that streptococcal infections in Yemen peaked during the winter months (November and December) and the rainy season (July and August). The increased prevalence during colder months may be attributed to environmental conditions that favor the survival and multiplication of the microorganism.

Antimicrobial Susceptibility

One of the main objectives of the present study was to evaluate the sensitivity and resistance patterns of *Streptococcus pyogenes* isolates against antibacterial drugs commonly available in the Yemeni market. The results demonstrated that *S. pyogenes* isolates were sensitive to most of the tested antibiotics, including Penicillin G, Amoxicillin, Ampicillin, Cefotaxime, Cephalosporins, Ceftriaxone, Lincamycin, and Vancomycin. These findings are consistent with previous studies (Stevens, 1995; Shulman et al., 2012; Ba-Saddik et al., 2014; Krohn et al., 2018; Khalaf et al., 2020; Helal et al., 2020). In contrast, resistance was observed against Streptomycin, Gentamycin, Levofloxacin, Tetracycline, Erythromycin, and Clindamycin, which aligns with the results reported by other researchers (Olivieri et al., 2015; Michos et al., 2016; Vela et al., 2017; Khalaf et al., 2020). The resistance of *S. pyogenes* to certain antibacterial agents may be attributed to factors such as the overuse and misuse of antibiotics, impaired cellular uptake of the drugs, or the emergence of mutant strains (Adesola, 2012).

CONCLUSION

It could be concluded from findings of study that, *S.pyogenes* was found to be prevalent among the population in the study areas, and bacterial resistance to antimicrobial agents was observed. It is therefore recommended that routine testing for antibiotic resistance be conducted for drugs prescribed to both humans and

animals. Additionally, further research is needed to investigate the epidemiology of *Streptococcus* infections in other regions of study areas.

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DATA AVAILABILITY

The data are available within text of the article.

ETHICAL CONSIDERATIONS

The study received approval from the Faculty of Veterinary Medicine, Thamar University. Informed consent, either verbal or written, was obtained from all adult participants, as well as from the parents or guardians of children, prior to the collection of samples**.**

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests or conflicts of interest that could have influenced the results or the publication of this work.

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المكورات العقدية المقيحة في الانسان في ذمار، اليمن: معدل الانتشار وأنماط الحساسية للمضادات الحيوية

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الملخص

تم إجراء هذه الدراسة المستعرضة القطاع في مناطق مختلفة من محافظة ذمار خلال الفترة بين 2024-2025 لتحديد انتشار المكورات العقدية القيحية في الإنسان، والعوامل المرتبطة بها وأنماط الحساسية الدوائية للسلالات المعزولة. تم جمع ما مجموعه 381 مسحة من الحلق من المشاركين من مختلف مناطق ذمار، محافظة ذمار. تم نقل العينات إلى المختبر في كلية الطب البيطري بجامعة ذمار حيث تم إجراء الزراعة الميكروبيولوجية والاختبارات الكيميائية الحيوية. كشفت النتائج أنه من بين 381 مسحة فموية/الحلق تم فحصها، كانت 67 (17.59%) إيجابية للإصابة بالمكورات العقدية القيحية. تم تسجيل أعلى معدل انتشار في منطقة رباط القلعة (4.72%)؛ في حين كان أدنى معدل في رخمة (0.26%). تم تسجيل أعلى معدل انتشار في الفئة العمرية من 5–15 سنة (7.61%)، بينما كان أدنى معدل في الفئة العمرية > 45 سنة ومافوق (2.36 %). تم تسجيل أعلى معدل انتشار في أكتوبر (4.99%)، في حين كانت النسبة أقل في مارس (0.79%). احصائيا، لوحظت فروق ذات دلالة معنوية ($P < 0.05$) بين انتشار المكورات العقدية وعوامل الشهر ومنطقة الدراسة. كشفت اختبارات التحسس للمضادات الحيوية أن سلالات *S. pyogenes* المعزولة كانت حساسة للبنسلين G، والأموكسيسيلين، والأمبيسيلين، والسيفوتاكسيم، والسيفالوسبورين، والسيفترياكسون، واللينكوميسين، والفانكومايسين بينما كانت مقاومة لكل من الستريتومايسين، والجنتاميسين، والليفوفلوكساسين، والتيتراسايكلين، والإريثروميسين، والكليندامايسين. خلصت الدراسة الى ان المكورات العقدية القيحية *S. pyogenes* منتشرة في مناطق الدراسة. وتوصي الدراسة بإجراء اختبار دوري للمضادات الحيوية الموصوفة للبشر والحيوانات، واجراء المزيد من الدراسات حول وبائيات المكورات العقدية القيحية في مناطق أخرى من محافظة ذمار.

الكلمات المفتاحية: المكورات العقدية *S. pyogenes*، مقاومة المضادات الحيوية، ذمار، اليمن.

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Full Length Article

تقييم نسبة حمض اليوريك إلى الكرياتينين في الدم كمؤشر للاعتلال الكلوي المبكر لدى مرض السكري من النوع الثاني: دراسة ميدانية في صنعاء، اليمن

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الملخص

داء السكري هو اضطراب أيضي مزمن يتميز بضعف تنظيم مستوى سكر الدم. يؤدي ارتفاع سكر الدم المستمر إلى إحداث ضرر جهازي في أجهزة القلب والأوعية الدموية والكلى والعين والأعصاب والأوعية الدموية. يعتبر الاعتلال الكلوي السكري أحد المضاعفات الخطيرة لمرض السكري من النوع الثاني مرتبطًا بارتفاع مستويات حمض اليوريك والكرياتينين في الدم، وهي مؤشرات حيوية تشير إلى خلل كلوي مبكر. أجريت هذه الدراسة العرضية القطاع في مستشفى الثورة العام ومستشفى الجمهوري التعليمي (صنعاء- اليمن)، لدراسة العلاقة بين حمض اليوريك والكرياتينين في الدم ووظائف الكلى لدى مرضى السكري من النوع الثاني، تم اختيار 125شخصا منهم 100 مريض بالسكري، و25 شخصًا من الأصحاء. تم تقسيم المشاركين إلى خمس مجموعات كل مجموعة تحتوي على 25 شخصا: أربع مجموعات علاجية (العلاج الأحادي، والعلاج المركب والعلاج بالأنسولين، العلاج بالحمية الغذائية)، ومجموعة السيطرة (اشخاص اصحاء). تم تجميع العينات الدموية من كل المشاركين وفحصها مخبريا وفقا لطرق الفحص المعيارية. اظهرت نتائج الدراسة، أن المجموعة الاولى كشفت عن أفضل النتائج، مع انخفاض ملحوظ في ومستوى حمض اليوريك الى الكرياتنين (6.35 ملغ/ديسيلتر) مقارنة بالمجموعات العلاجية الأخرى ومجموعة السيطرة. اما المجموعات العلاجية الأخرى فقد سجلت قيم متفاوت لمستويات حمض اليوريك الى الكرياتنين وهي: 8.95، 12.95 ، 9.32، 7.65% لكل من المجموعة الثانية و الثالثة والرابعة ومجموعة السيطرة على التوالي . احصائيا، لوحظت فروق معنوية ذو دلالة معنوية ($P<0.05$) بين المجموعة الثالثة (الانسولين) والمجموعات العلاجية الأخرى ومجموعة السيطرة. نستنتج من هذه الدراسة ان قياس قيمة حمض اليوريك إلى الكرياتينين تمثل طريقة واعدة كمؤشر محتمل قد يساعد في اكتشاف الخلل الكلوي المبكر أو التشوهات الأيضية قبل حدوث ضرر أكثر لمريض السكري.

الكلمات المفتاحية: الكرياتينين، حمض اليوريك، الكلى، اليمن، مرض السكري.

المقدمة INTRODUCTION

يُعد داء السكري (DM) أحد أكثر الأمراض المزمنة انتشارًا حول العالم، حيث يؤثر حاليًا على أكثر من 537 مليون شخص على مستوى العالم وينتشر بسرعة هائلة في المجتمع (Saeedi et al., 2019). هناك عدة انواع من مرض السكري، منها النوع الأول، والنوع الثاني، سكري الحمل، والسكري المناعي الذاتي الكامن لدى البالغين (LADA)، وسكري الشباب الناضجين (MODY)، وهو شكل وراثي ونادر من السكري.

اما أسباب وعوامل الخطورة المصابة للإصابة بالسكري فهي متعددة منها العوامل الوراثية ونمط الحياة، والخمول البدني (Khan et al., 2023, Fang et al., 2023)، والعوامل الطبية والبيئية. تزيد العوامل الوراثية مثل تاريخ العائلة وبعض الطفرات (مثل MODY) من خطر الإصابة بالسكري (Alam et al., 2022). وتساهم العوامل البيئية بشكل كبير في تطور المرض (Lin and Li 2021) مثل تلوث الهواء والتعرض للمبيدات الحشرية ونقص فيتامين (د) (Beulens et al., 2022, and Khalil et al., 2023). كما أظهرت دراسات وبائية أن السمنة من اهم عوامل الخطورة للإصابة بمرض السكري من النوع الثاني (Mohajan and Haradhan 2023).

وسكرى النوع الثاني هو الأكثر شيوعًا من أمرض السكري، والسبب في ذلك هو مقاومة الأنسولين وضعف إفراز الأنسولين بسبب

خلل وظيفي في وظيفة خلايا بيتا، حيث يمثل أكثر من 90٪ من جميع حالات السكري في جميع أنحاء العالم (Sun et al., 2022). وينتج عن ذلك أكثر من مليون حالة وفاة، وأصبح السكري سابع مرض مسببا للوفاة في العالم (Khan et al., 2020). يؤثر ارتفاع سكر الدم وما يرتبط به من اضطرابات أيضية على أعضاء متعددة من الجسم ويعطل أداءها الطبيعي وفي النهاية فشل الأعضاء مثل اضطرابات العينين والكلى والقلب والأعصاب (Siddiqui et al., 2024).

مرض السكري من النوع الثاني مهم لأنه شائع وله مضاعفات خطيرة، ويرتبط بعوامل سلوكية وبيئية ومجتمعية مثل زيادة الوزن والنشاط البدني والسلوك الخامل والعادات الغذائية غير الصحية (Khan et al., 2023). يُقدر عدد المصابين به حوالي أكثر من 600 مليون في العالم في العام 2023م. ومن المتوقع يكون 642 مليون شخص بحلول عام 2040 (Joline et al., 2022). أكثر من 90٪ المصابون بمرض السكري من النوع الثاني يعيش نصفهم في بلدين كبيرين هما الهند والصين ((Sun et al., 2022). اما في بلدان الشرق الأوسط ومنها اليمن فأعداد مرضى السكري أصبحت مصدر قلق للجميع، فمعدل انتشاره في اليمن بلغ 10.4٪، والمملكة العربية السعودية (23.7٪)، والأردن (17٪)). ويمكن الوقاية من حالات مرض السكري النوع الثاني من خلال تحسين عوامل الخطر الرئيسية القابلة للتحكم مثل السمنة، وقلة النشاط البدني، والنظام الغذائي غير الصحي (Schellenberg et al., 2013; Bellou et al., 2018).

إشارة بعض الدراسات الحديثة عن وجود علاقة بين فرط حمض اليوريك ، وتركيز الكرياتينين وامراض القلب والأوعية الدموية وأمراض الكلى المزمنة ومرض السكري في الانسان Yanai et al., 2021; Nakayama et al., 2023; Wen et al., 2024). حيث أظهرت دراسة تشن لي (Chunlei et al., 2019) أن نسبة حمض اليوريك في الدم إلى الكرياتينين (SUA/SCr) هي مؤشر ذو قيمة علمية للتنبؤ بمرض الكلى في المرضى الذين يعانون من داء السكري من النوع الثاني (Tao et al., 2020). وبالتالي يمكن لنسبة SUA/SCr أن تقدم معلومات جديدة لشرح الارتباط بين SUA ومرض الكلى المزمن، وعلى حسب علمنا لم يتم بعد تقييم العلاقة بين SUA/SCr ومرض الكلى المزمن لدى مرض السكرى باليمن، لذا هدفت هذه الدراسة تقييم مستوى نسبة حمض اليوريك إلى الكرياتينين لدى مرضى السكري من النوع الثاني كمؤشر حيوي في اكتشاف الخلل الكلوي المبكر في مرض السكري في مدينة صنعاء، اليمن.

المواد وطرق العمل Materials & Methods

منطقة الدراسة ومجتمع الدراسة

هدفت هذه الدراسة التحليلية العرضية القطاع الى التحقيق في تقييم نسبة حمض اليوريك إلى الكرياتينين كمؤشر حيوي في مرض السكري من النوع الثاني. أجريت الدراسة في بعض مستشفيات في صنعاء، اليمن، وقد شملت هيئة المستشفى الجمهوري التعليمي ومستشفى الثورة العام النموذجي خلال الفترة 2024-2025م. تم اختيار هذه المستشفيات بسبب العدد الكبير من مرضى السكري الذين يزورونها بصفة مستمرة للكشف الروتيني والعلاج.

حجم العينة وتصميم الدراسة وجمع البيانات

تكون مجتمع الدراسة من 125 مشاركًا، تم حساب حجم العينة باستخدام برنامج G-power (الإصدار 3.1) بناءً على حجم تأثير متوقع للعينات (f=0.3) لتحليل التباين (ANOVA)، مع خطأ $\alpha = 0.05$ وقوة (1-β) 80٪، مما أدى إلى الحد الأدنى المطلوب للعينة وهو 125 مشاركًا من مرضى السكر النوع الثاني.

تم تقسيم المشاركين إلى خمس مجموعات، وكل مجموعة شملت على 25 مشاركا كالاتي: المجموعة الاولى تم اعطاءها العلاج المركب (جلوكوفاز، Metformin, Glucovance 500mg/5mg hydrochloride and Glibenchlamide)، المجموعة الثانية تم اعطاءها العلاج الأحادي (ميتافورمين، Metformin 500 mg) ، المجموعة الثالثة تم اعطاءها الانسولين، المجموعة الرابعة تم اخضاعها لنظام غذائي منظم(حمية)، والمجموعة الخامسة شملت مشاركون بالغون أصحاء متطابقون في العمر والجنس وليس لديهم تاريخ للإصابة بالسكري أو أمراض الكلى كمجموعة ضابطة.

تم جمع البيانات المطلوبة للدراسة باستخدام استبيان تضمن كلاً من الأسئلة المغلقة (نعم/لا) والتي شملت 10 أسئلة، والأسئلة المفتوحة والتي شملت 5 أسئلة لالتقاط البيانات الكمية والنوعية. تألف الاستبيان من 15 سؤالاً أساسياً مقسمة إلى ثلاث محاور هي: عوامل نمط الحياة (شملت حالات التدخين، النشاط البدني والنظام الغذائي)، التاريخ الطبي (وشمل تشخيص مرض، التاريخ العائلي، تاريخ الإصابة، إجراء اختبارات HbA1c والكرياتينين/حمض اليوريك).، والالتزام بالعلاج (وشمل استخدام ادوية السكر والأدوية الخافضة لحمض اليوريك/الكرياتينين).

تجميع العينات البيولوجية وتحليلها

تم جمع 3 مل من الدم من كل مشارك. قبل البدء في عملية سحب الدم، تم تنظيف المنطقة التي سحبت منها العينة في اليد بمادة كحولية، تم سحب الدم كما هو معمول به في عملية تجميع العينات وفقا للقواعد العلمية والصحية بوتيرة معتدلة لتجنب انحلال الدم (تدمير خلايا الدم الحمراء)، والذي يمكن أن يؤثر على نتائج الاختبارات. بعد جمع الدم في انابيب ((Serum-separating tubes (SSTs) المحتوية على الجل، تركت العينة في درجة حرارة الغرفة للسماح لها بالتجلط. وبعد تكوين الجلطة، تم استخدام جهاز الطرد المركزي CGOLDENWALL (2-80) لفصل المصل بسرعة 3500 دورة في الدقيقة لمدة 15 دقيقة. تم نقل المصل إلى أنابيب ابندروف (Eppendorf)، وحفظها في الثلاجة عند درجة حرارة 2-8 درجة مئوية لحين اجراء الاختبارات الكيميائية الحيوية المطلوبة باستخدام جهاز قياس الطيف الضوئي:(Spectrophotometer) - V-1000 من شركة (AOE Instruments، شنغهاي، الصين) وفقا لتعليمات الشركة المصنعة.

قياس سكر الدم والسكر التراكمي:

تم قياس مستويات سكر الدم الصائم، سكر الدم التراكمي لدى المشاركين في الدراسة وفقا لطريقة (2023) .Ansari et al.

قياس حمض اليوريك والكرياتينين

تم قياس حمض اليوريك في الدم لدى المشاركين في الدراسة باستخدام أدوات محلول إنزيم اليوريكيز (Química Clínica Aplicada S.A، إسبانيا) وفقا تعليمات الشركة المصنعة، وقياس الكرياتينين، باستخدام طريقة Jaffe kinetic method، Química Clínica Aplicada S.A، إسبانيا) وفقا لتعليمات لشركة المصنعة. تم شراء جميع المواد الكيميائية والأجهزة من السوق المحلية لشركات الادوية والمستلزمات الطبية من مدينة صنعاء، اليمن.

التحليل الإحصائي

تم إجراء التحليل الإحصائي باستخدام برنامج IBM SPSS Statisticsالإصدار 21 .جرى حساب القيم لكل مجموعة على شكل المتوسط الحسابي ± الانحراف المعياري (SD) .كما تمت مقارنة المتوسطات بين المجموعات الخمس قيد الدراسة باستخدام تحليل التباين الأحادي (ANOVA)، مع اعتبار النتائج ذات دلالة إحصائية عند مستوى احتمالية 0. 05 ≥ P.

الاعتبارات الأخلاقية

تم الحصول على موافقة جامعة آزال للتنمية البشرية لإجراء الدراسة رقم (24/113- 2024/10)، وعلى موافقة جميع المشاركين من

المرضى المترددين على عيادة مرض السكري في مستشفى الجمهوري والثورة قبل اخذ العينات. تم ابلاغ كل المشاركين بان المعلومات المتحصل عليها ستحفظ بسرية تامة ولغرض الدراسة فقط.

النتائج والمناقشة Results & Discussion

داء السكري هو اضطراب أيضي مزمن يتميز بضعف تنظيم مستوى الجلوكوز في الدم. يؤدي ارتفاع السكر في الدم المستمر إلى إحداث ضرر جهازي في أجهزة القلب والأوعية الدموية والكلى والعين والأعصاب والأوعية الدموية. يعتبر الاعتلال الكلوي السكري أحد المضاعفات الخطيرة لمرض السكري من النوع الثاني مرتبطًا بارتفاع مستويات حمض اليوريك والكرياتينين في الدم، وهي مؤشرات حيوية تشير إلى خلل كلوي مبكر. أجريت هذه الدراسة الميدانية في مستشفى الثورة العام ومستشفى الجمهوري التعليمي (صنعاء- اليمن)، لدراسة العلاقة بين حمض اليوريك في الدم والكرياتينين ووظائف الكلى على مرضى بالسكري من النوع الثاني، الجدول رقم (1) يعرض الخصائص لأساسية للمشاركين في الدراسة.

قياس مستوى الجلوكوز في الدم (سكر الدم الصائم)

كشفت نتائج هذه الدراسة ان متوسط مستوى الجلوكوز (سكر الدم الصائم) في مجموعة الاولى (العلاج المركب) كان 58±202 ملغ/ديسيلتر، والمجموعة الثانية (العلاج بالميتفورمين) 62214± ملغ/ديسيلتر، مع قيم تتراوح من 96 ملغ/ديسيلتر إلى 355 ملغ/ديسيلتر، والمجموعة الرابعة (النظام الغذائي) والخامسة (السيطرة) سجلتا مستويات ادنى في مستويات الجلوكوز او سكر الدم وهي 74±173 و36±103 ملغ/ديسيلتر على التوالي، وكما هو موضح بالجدول رقم (2) . تعكس هذا النتائج نطاق واسعا وتباينًا كبيرًا في استقرار نسبة السكر في الدم بين المرضى المشاركين. ويعزو ارتفاع الجلوكوز لدى بعض المشاركين، ربما الى سوء العادات الغذائية، أو الخمول البدني، أو الجرع غير الكافية من ادوية الخافضة والمعالجة للسكرى. اما المجموعة الثالثة (المعالجة بالأنسولين) فقد سجلت أعلى متوسط للجلوكوز (70±232ملغ/ديسيلتر) مقارنة من المجموعات الدراسة الاخريات ومجموعة السيطرة، مع مدى يتراوح من (131.24 ملغ/ديسيلتر إلى 383.8 ملغ/ديسيلتر). قد تُعزى هذه التقلبات في قيم سكر الدم او الجلوكوز لدى المشاركين في المجموعة الثالثة إلى عدم الانتظام في جرعات الأنسولين، أو توقيت تناوله، أو العادات الغذائية، أو مدى الالتزام بتناول بالعلاج او التدخين. اتفقت نتائج هذه الدراسة مع دراسة (Khan et al., 2023)، واختلفت مع دراسة (Čaušević et al, 2010). احصائيا، كانت هناك فروق معنوية ذات دلالة إحصائية (P<0.05) بين المجموعة الثالثة وبقية مجموعات الدراسة ومجموعة السيطرة.

مستوى السكر التراكمي في الدم (HbA1c)

الجدول رقم (3) يوضح نتائج قياس مستويات السكرى التراكمى لدى مرضي السكرى من النوع الثاني، أظهرت النتائج أن قيم مستويات متوسطات السكر التراكمي (HbA1c) في المجموعة الأولى والمجموعة الثانية كانت 1.95±8.73، و 2.2±9.02 على التوالي، في حين وصلت القيمة القصوى المسجلة إلى 14٪، وهي أعلى بكثير من الهدف الموصي به لمرضى السكري (عادةً <7٪). يشير هذا النطاق الواسع إلى أنه في حين حافظ بعض المرضى على تحكم مقبول في نسبة السكر في الدم، عانى آخرون من اختلال كبير في التنظيم. قد تشمل العوامل المساهمة والمحتملة في تباين القيم المسجلة لمستويات السكر التراكمي لدى المشاركين، عدم الانتظام في تناول الدواء أو الاستجابات الفردية المختلفة للعلاج.

اما في المجموعة الثالثة، فقد كان متوسط مستوى السكر التراكمي (2.5% ± 9.7)، في حين كانت اعلى قيمة مسجلة بلغت (15.0٪) . ربما يعزو السبب في ذلك الى عدة عوامل مثل مقاومة الأنسولين الشديدة، وعدم انتظام تناول الأنسولين، والسمنة، وضعف الالتزام ببروتوكولات العلاج حسب إرشادات الطبيب. اتفقت نتائج هذه الدراسة مع دراسة (Xing et al, 2022)، التي وجدت ارتباط أقوى لدى المشاركين الذين لديهم سمنة ومستوى السكر التراكمي كان (7%>) ، كما وجد (Smith et al., 2020; Minari et al., 2023) أيضًا أن الأنسولين وحده دون تغيير متزامن في نمط الحياة قد يكون غير كافٍ لتحقيق أهداف التحكم بسكر الدم. اما قيم مستويات السكر التراكمي في المجموعتين الرابعة وفي الخامسة فقد كانت في الحدود الطبيعية. كشفت نتائج التحليل الاحصائي ان هناك فروق معنوية (P<0.05) بين مجموعة السيطرة وبقية مجموعات الدراسة الأخرى.

مستوى الكرياتينين

أظهرت النتائج في الجدول (4) ان متوسط مستوى الكرياتينين في المجموعة الأولى كان 0.92 ± 0.37 ملغ/ديسيلتر، مع تسجيل أعلى قيمة عند 1.67 ملغ/ديسيلتر. في حين يقع المتوسط العام ضمن النطاق الطبيعي، فإن القيم المرتفعة لدى مجموعة فرعية من المرضى تثير مخاوف بشأن احتمال وجود قصور كلوي. قد ترتبط هذه الارتفاعات بارتفاع سكر الدم طويل الأمد وبداية الاعتلال الكلوي السكري.

بلغ قيمة متوسط مستوى كرياتينين في المجموعة الثانية (1.7±1.23 ملغ/ديسيلتر)، تشير هذه النتائج إلى إجهاد كلوي محتمل ، وتتفق هذا النتائج مع ما توصل الي (Smith et al., 2020) و الذى اكد على أن ضعف التحكم في نسبة السكر في الدم حتى تحت العلاج يمكن أن يساهم في مضاعفات كلوية طويلة الأجل.

بلغ قيمة متوسط مستوى الكرياتينين في مجموعة الثالثة 0.30±0.8 ملغ/ديسيلتر، مع قيمة قصوى بلغت 1.36 ملغ/ديسيلتر. على الرغم من أنها تقع عمومًا ضمن الحدود العليا للنطاق الطبيعي، إلا أن القراءات المرتفعة في بعض الحالات قد تشير إلى علامات مبكرة للقصور الكلوي، والتي قد تتفاقم بسبب العبء الأيضي المزمن لمرض السكري أو الاستخدام طويل الأمد للأنسولين. لوحظت أدنى متوسطات لمستويات الكرياتينين في الرابعة(0.3107± ملغ/ديسيلتر) ، مما قد يشير إلى تحسن في وظائف الكلى مرتبط بانخفاض استهلاك البروتين. ومع ذلك، يجب تفسير هذا بحذر، نظرًا لوجود قيم مرتفعة للكرياتينين لدى بعض الأفراد.

مستوى حمض اليوريك

أظهرت النتائج الواردة في الجدول (4) أن متوسط مستوى حمض اليوريك في المجموعة الاولى بلغ 4.33±8.25 ملغ/ديسيلتر. كما لوحظ أن أحد المرضى في هذه المجموعة سجّل قيمة مرتفعة بشكل غير طبيعي بلغت 38.6ملغ/ديسيلتر، وهي أعلى بكثير من النطاق المعتاد لهذه المجموعة. ويمكن تفسير هذه القيمة الشاذة بعدة احتمالات، منها: خطأ ما قبل التحليل مثل انحلال الدم أو سوء التعامل مع العينة، وجود اضطراب أيضي غير مشخص مثل متلازمة ليش-نيهان أو خلل مشابه في استقلاب البيورين، أو الاستخدام المتزامن لمدرات البول التي قد ترفع مستويات حمض اليوريك في الدم. ونظرًا للطبيعة القصوى لهذه النتيجة، فقد تم استبعادها من حساب المتوسطات لتجنب تحريف البيانات، مع التأكيد على ضرورة المتابعة السريرية لاحتمال وجود حالة مرضية كامنة خطيرة.

من ناحية أخرى، بلغ متوسط مستوى حمض اليوريك في المجموعة الثالثة 7.71±7.95ملغ/ديسيلتر، وهو أعلى بشكل ملحوظ مقارنةً بالمجموعات الأخرى، باستثناء مجموعة الاولى التي سجلت قيمة مقاربة. أما مجموعتا الحمية(الرابعة) والضابطة(الخامسة) فقد أظهرتا مستويات أقل من باقي المجموعات، كما هو موضح في الجدول (4). إحصائيًا، لوحظ وجود فروق معنوية (P<0.05) ذو دلالة احصائية بين المجموعة الاولى والثالثة مقارنةً بالمجموعة الخامسة (الضابطة) وتشير هذه النتائج إلى أن المجموعات الأولى، والثانية، والثالثة هي الأكثر عرضة لتأثير حمض اليوريك على وظائف الكلى. كما أن ارتفاع مستوى حمض اليوريك في الدم يُعد عامل خطر مستقل لانخفاض وظائف الكلى

حتى لدى الأفراد الأصحاء ذوي ضغط الدم الطبيعي، وهو ما يتفق مع ما ورد في دراسات Luo وآخرين (2024) و Bellomo وآخرين(2010) .

نسبة حمض اليوريك إلى الكرياتينين (SUA/Cr)

أظهرت نتائج الجدول (4) أن أعلى قيمة لمستوى الكرياتينين إلى حمض اليوريك (SUA/Cr) سُجلت في المجموعة الثالثة (12.95 ملغ/ديسيلتر)، مقارنة ببقية المجموعات ومجموعة السيطرة. ويشير ذلك إلى تأثير محتمل للعلاج بالأنسولين في رفع مستويات حمض اليوريك أو تقليل إفرازه الكلوي، وهو ما يتفق مع ما ورد في دراسة للباحث جو وآخرون (Gu et al., 2017). في المقابل، سجلت الاولى أقل قيمة (6.35 ملغ/ديسيلتر)، مما يعكس فعالية علاجية واضحة في خفض نسبة SUA/Cr وتحسين وظائف الكلى. أما المجموعتان الثانية والرابعة، فقد أظهرت قيم مرتفعة نسبيًا لمستوى الكرياتينين إلى حمض اليوريك وهي 8.95 ملغ/ديسيلتر و9.31 ملغ/ديسيلتر على التوالي مقارنة بمجموعة السيطرة، وهو ما يبرز محدودية تأثير مجموعتي العلاج والنظام الغذائي كل على حده في ضبط المؤشرات الحيوية الكلوية. تتفق هذه النتائج مع ما أشار اليه الباحث (Chunlei et al., 2019) وآخرون، حول القيمة التنبؤية لقيمة SUA/Cr باعتبارها مؤشرًا مستقلًا وغير جراحي لتدهور وظائف الكلى لدى مرضى السكري من النوع الثاني، خصوصًا في البيئات محدودة الموارد مثل اليمن. إحصائيًا، لوحظ وجود فروق معنوية ذات دلالة إحصائية (P<0.05) بين مجموعة العلاج بالأنسولين والمجموعة الضابطة.

الاستنتاجات :Conclusions

نستنتج من نتائج الدراسة ان قياس قيمة حمض اليوريك إلى الكرياتينين تمثل طريقة واعدة كمؤشر محتمل قد يساعد في اكتشاف الخلل الكلوي المبكر أو التشوهات الأيضية قبل حدوث ضرر أكثر لمريض السكري.

الجدول (1): يوضح الخصائص الأساسية لمجموعات المشاركين في الدراسة

المجموعة العلاجية	توزيع الفئات العمرية (سنة)	العادات الغذائية	متوسطات المؤشرات الصحية
الاولى (العلاج بمنظم السكر جلوكوفاز)	اقل من 40 سنة (24%) من 41-60 سنة (60%) اكثر من 61 سنة (14%)	نظام غذائي غير منتظم (60%)	HbA1c: 8.73% Uric acid: 8.25 mg/dl Creatinine:0.92 mg/dl
الثانية (العلاج بالميتفورمين)	اقل من 40 سنة (24%) من 41-60 سنة (60%) اكثر من 61 سنة (14%)	تحكم جزئي في النظام الغذائي (45%)	HbA1c: 9.02% Uric acid: 7.82 mg/dl Creatinine:1.23 mg/dl
الثالثة (العلاج بالأنسولين)	اقل من 40 سنة (28%) من 41-60 سنة (44%) أكثر من 61 سنة (28%)	نظام غذائي متوافق مع العلاج(30%)	HbA1c: 9.7% Uric acid: 9.5 mg/dl Creatinine:0.8 mg/dl
الرابعة (النظام الغذائي)	اقل من 40 سنة (48%) من 41-60 سنة (40%) أكثر من 61 سنة (12%)	عادات غير منظمة (100%)	HbA1c: 7.65% Uric acid: 6.49 mg/dl Creatinine:0.7 mg/dl
الخامسة (السيطرة)	اقل من 40 سنة (72%) من 41-60 سنة (24%) اكثر من 61 سنة (4%)	غذاء صحي (80%)	HbA1c: 5.4% Uric acid: 6.27 mg/dl Creatinine: 0.82 mg/dl

الجدول (2): يوضح مستوى الجلوكوز او سكر الدم الصائم ملغ/ديسيلتر في مرض السكرى من النوع الثانى

المجموعات العلاجية	المتوسط ± SD (mg/dL)	الذكور (mg/dL)	الاناث (mg/dL)	أكبر قيمة (mg/dL)	اقل قيمة (mg/dL)
الاولى (العلاج بمنظم السكر جلوكوفاز)	202±58b	212	188	297	96
الثانية (العلاج بالميتفورمين)	214±62b	182	248	355	134
الثالثة (العلاج بالأنسولين)	232±70 c	228	236	383	131
الرابعة (النظام الغذائي)	173±74b	193	154	383	99
الخامسة (السيطرة)	103±36a	102	117	191	65

الأحرف المختلفة ضمن العمود الواحد تشير الى وجود فروق معنوية (P<0.05)بين متوسطات المعاملات

الجدول (3): يوضح مستوى السكر التراكمي لدى المشاركين في الدراسة

المجموعة	المتوسط±SD	الذكور(%)	الاناث (%)	أكبر قيمة (%)	اقل قيمة (%)
الاولى (العلاج بمنظم السكر جلوكوفاز)	8.73±1.95b	9.1	8.25	12.5	5.9
الثانية (العلاج بالميتفورمين)	9.02±2.2bc	8	10.12	14	6.3
الثالثة (العلاج بالأنسولين)	9.7±2.5c	9.58	9.86	15	6.2
الرابعة (النظام الغذائي)	7.65±2.6b	8.37	6.99	15	5.1
الخامسة (السيطرة)	5.4±0a	5.4	5.5	5.5	5.4

الأحرف المختلفة ضمن العمود الواحد تشير الى وجود فروق معنوية (P<0.05)بين متوسطات المعاملات

الجدول (4): نسبة حمض اليوريك إلى الكرياتينين لدى مجموعات الدراسة

المجموعة	الكرياتين (Cr) (mg/dL)	حمض اليوريك (SUA) (mg/dL)	SUA/CrMg/dL
الاولى (العلاج بمنظم السكر جلوكوفاز)	0.92±0.37 ab	8.25±4.33 b	6.35a
الثانية (العلاج بالميتفورمين)	1.23±1.7 b	7.82±5.34 ab	8.95ab
الثالثة (العلاج بالأنسولين)	0.8±0.30 ab	7.95±5.03 b	12.95c
الرابعة (النظام الغذائي)	0.7±0.31 a	6.49±4.68 a	9.32b
الخامسة (السيطرة)	0.8±0.30 ab	6.27±2.44 a	7.65ab

الأحرف المختلفة ضمن العمود الواحد تشير الى وجود فروق معنوية (P<0.05)بين متوسطات المعاملات

الشكر والعرفان

يتقدم الباحثون بالشكر والتقدير للأستاذ الدكتور/عادل نعمان عميد كلية العلوم الطبية بجامعة آزال على دعمه وتسهيل إجراءات الدراسة. كما نشكر الدكتور محمد راشد رئيس قسم المختبرات بجامعة آزال على تقديم المعلومات والنقاش المفيد اثناء أداء البحث.

مصدر التمويل

لا يوجد أي مصدر للتمويل وكان التمويل شخصي من الباحثين.

اسهامات الباحثين

الباحث حميد محمد الجبر: شارك في كتابة البحث واجراء التحليل الاحصائي والاشراف على جمع العينات وتحليلها في المختبر. الباحثون: غدير منصور الشاوش؛ أحمد عبد الله رزوم، سندس يحيى الفقيه؛ مها جمال محسون؛ آية احمد أنعم؛ ندى صالح الشريف؛ سمية أحمد اليافعي؛ ليلى محسن القطيبي؛ عفاف عمر الحداد؛ عائشة عبد السلام شايع؛ مروة محمد العزي؛ رويدا هلال المقبلي؛ أصيل احمد العنس؛ منير محمد العنس: شاركوا بجمع العينات (الدم)، وجمع بيانات الشخصية من مرضى السكري، كتابة البحث، وجمع المادة العلمية.

تضارب المصالح

يؤكد الباحثون انه لا يوجد تضارب للمصالح جراء اجراء هذا البحث.

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Evaluation of serum uric acid to creatinine ratio as a biomarker in type 2 diabetes mellitus in Sana'a city, Yemen

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ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by impaired regulation of blood sugar levels. Persistent hyperglycemia leads to systemic damage affecting the cardiovascular system, kidneys, eyes, nerves, and blood vessels. Diabetic nephropathy is one of the serious complications of type 2 diabetes, associated with elevated levels of uric acid and creatinine in the blood, which are vital biomarkers indicating early renal impairment. This cross-sectional study was conducted at Al-Thawra General Hospital and Al-Jumhuri Teaching Hospital (Sana'a, Yemen) to investigate the relationship between blood uric acid and creatinine levels and kidney function in patients with type 2 diabetes. A total of 125 individuals were selected, including 100 diabetic patients and 25 healthy subjects. Participants were divided into five groups, each containing 25 individuals: four treatment groups (monotherapy, combination therapy, insulin therapy, and dietary therapy) and one control group (healthy individuals). Blood samples were collected from all participants and analyzed in the laboratory according to standard examination methods. The study results showed that the first group revealed the best outcomes, with a significant reduction in the uric acid-to-creatinine ratio (6.35 mg/dL) compared to the other treatment groups and the control group. The other treatment groups recorded varying values of the uric acid-to-creatinine ratio: 8.95, 12.95, 9.32, and 7.65% for the second, third, fourth, and control groups, respectively. Statistical differences ($P<0.05$) were observed between third group and other treated group and control. We concluded from this study that measuring the uric acid-to-creatinine ratio represents a promising method as a potential biomarker that may help in detecting early renal impairment or metabolic abnormalities before more severe damage occurs in diabetic patients.

Keywords: Creatinine, Diabetes Mellitus, Kidney, Uric acid, Yemen

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Full length article

Cypermethrin–Induced Nephrotoxicity in Rabbits: A Histopathological Study

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ABSTRACT

Cypermethrin is an important type II pyrethroid pesticide widely used to protect crops against pests and insect infestations, but it is also associated with environmental pollution and health hazards. The present study was designed to investigate histological changes in the kidneys of male rabbits following exposure to cypermethrin. A total of 18 adult male rabbits were used. The rabbits were randomly divided into three groups of six animals each. The first group(G1) served as the control and received normal saline daily. The second group(G2) was administered cypermethrin orally at a dose equivalent to 1/10 of the LD_{50} (66.5 mg/kg body weight) once daily for 21 consecutive days. The third group(G3) received a higher oral dose equivalent to 1/5 of the LD_{50} (133 mg/kg body weight) under the same schedule. Histological examination of the treated groups revealed multiple pathological alterations compared to control group, Cypermethrin caused degeneration of renal corpuscles, hydropic changes, necrosis, inflammation, fatty degeneration, amyloidosis, dilation of renal tubules, congestion, fibrosis, steatosis, and tubular degeneration. In conclusion, cypermethrin produced significant histological damage in the kidneys of male rabbits. Further research is required to elucidate the molecular and cellular mechanisms underlying cypermethrin-induced nephrotoxicity.

Keywords: Cypermethrin, Histopathological**,** Kidney, Toxicity, Rabbits.

INTRODUCTION

Pyrethroids, synthetic derivatives of natural pyrethrins, represent the most widely used class of pesticides globally due to their high efficacy, relatively low mammalian toxicity, and rapid biodegradation in the environment (Ahmad et al., 2009). They are generally classified into two groups: Type I (without an alpha-cyano group) and Type II (with an alpha-cyano group), which differ in their structural features and the behavioral effects they produce (Spencer et al., 2005; Wolansky et al., 2006; Saka et al., 2011). Despite their widespread use, pyrethroid pesticides, including cypermethrin, are recognized as major environmental pollutants. Cypermethrin toxicity has been documented in numerous experimental and clinical studies (Idris et al., 2012; USEPA, 2009; Singh et al., 2012).

Cypermethrin, a Type II pyrethroid, was first synthesized in 1974 and introduced commercially in 1979 (WHO, 1989). It has a high potential to accumulate within food chains, thereby contributing to toxic effects in exposed organisms (Muthuviveganandavel et al., 2011; Sangha et al., 2013). In humans, cypermethrin poisoning manifests as facial burning and tingling (paraesthesia), dizziness, headaches, nausea, anorexia, fatigue, and urinary incontinence. With higher exposure, symptoms may progress to muscle twitching, drowsiness, coma, and seizures (Chakravarthi et al., 2007; Gheshlaghi et al., 2011). In laboratory animals, toxic signs include pawing, burrowing, salivation, tremors, writhing, and seizures (Ullah et al., 2006; Grewal et al., 2010).

Kidney function can be assessed through the measurement of metabolic waste products such as urea

and creatinine, which are normally excreted via the renal system (Garba et al., 2007). Elevated levels of these metabolites in blood indicate cellular damage and impaired renal clearance (Aslam et al., 2010). Thus, urea and creatinine serve as sensitive biochemical markers for diagnosing renal injury. Reduced serum protein levels may result from renal or intestinal protein loss, hemorrhage, malabsorption, or liver dysfunction (Khan, 2008).

Exposure to cypermethrin has been linked to a wide range of adverse effects, including anemia, impaired blood coagulation, neurotoxicity, paralysis, jaundice, hepatic fibrosis, renal dysfunction, cancer, genetic abnormalities, birth defects, and reproductive disorders such as impotence and infertility (Yousef et al., 2003a,b). Long-term exposure has also been associated with dopaminergic neurodegeneration in adult rats (Singh et al., 2012). Several studies have demonstrated that cypermethrin induces diverse physiological, biochemical, toxicological, and histological alterations in experimental animals (Kumari et al., 2002; Hussain et al., 2009).

Although extensive research have addressed hepato-renal pathology in pyrethroid-exposed animals, humans, and environmental systems, the present study aims to provide a detailed description of kidney pathology in animals exposed to cypermethrin under local environmental conditions.

MATERIALS AND METHODS

This experimental study was conducted in the Department of Biology, Faculty of Education, University of Thamar, Yemen.

Experimental Animals

Eighteen mature healthy male rabbits (*Oryctolagus cuniculus*) weighing between 900–1200 g, were obtained from the local market of Dhamar, Yemen.

Chemicals

The synthetic Cypermethrin Pyrethroid (α-Cyano-3-phenoxy benzyl 3-(2, 2-dichloro vinyl)-2,2-dimethyl cyclopropane carboxylate). Cypermethrin(10% EC) produced by Vapco company- Amman Jordan and purchased from authorized dealers in local market at Dhamar, Yemen**.**

Study Design

The experimental animals were housed under uniform management conditions in the animal facility of the Biology Department, Faculty of Education, University of Thamar, Yemen. All animals were healthy and acclimatized for 14 days prior to the experiment.

The rabbits were randomly divided into three groups of six animals each. The first group(G1) served as the control and received normal saline daily via disposable syringe. The second group(G2) was administered cypermethrin orally at a dose equivalent to 1/10 of the LD50 (66.5 mg/kg body weight) once daily for 21 consecutive days. The third group(G3) received a higher oral dose equivalent to 1/5 of the LD50 (133 mg/kg body weight) under the same schedule. Cypermethrin was dissolved and diluted in distilled water to achieve the required concentrations.

Throughout the study, animals were maintained under daily observation in well-ventilated housing at room temperature (25–27°C), relative humidity (50 ± 15%), and a 12-hour light/dark cycle. They were provided with rabbit chow and water *ad libitum*, ensuring equal quantities of food and water across all groups.

2.5. Specimen processing and Histolopathological examination

At the end of the experiment, all rabbits were subjected to necropsy. Kidneys were excised, rinsed in normal saline, and fixed in 10% formalin for 24 hours. Following fixation, tissues were washed in tap water, dehydrated through ascending grades of ethanol, cleared in xylene, and embedded in paraffin wax (melting point 50–56°C). Paraffin blocks were sectioned at 6 µm thickness using a rotary microtome. The sections were stained with Harris hematoxylin and eosin, examined under a light microscope, and photographed using an automated photomicrographic system according the techniques described by Jaber and Al-Bakri (2018); Al-Hamawandy and Al-Bakri (2020); Jaber et al. (2020).

RESULTS

The findings of this study can be summarized as follows: Kidney sections from rabbits in the control group, which received physiological saline, displayed normal renal tubules and glomeruli (Figure 1). In the group treated with cypermethrin at a dose of 66.5 mg/kg body weight for 21 days, several pathological alterations were observed, including degeneration of renal corpuscles, hydropic changes, necrosis, inflammation, fatty degeneration, amyloidosis, dilation of renal tubules, congestion, and fibrosis (Figures 2–6). In contrast, rabbits exposed to the higher dose of cypermethrin (133 mg/kg body weight for 21 days) exhibited marked histological changes such as steatosis, inflammation, degeneration of kidney tubules, and amyloidosis (Figures 7–8).

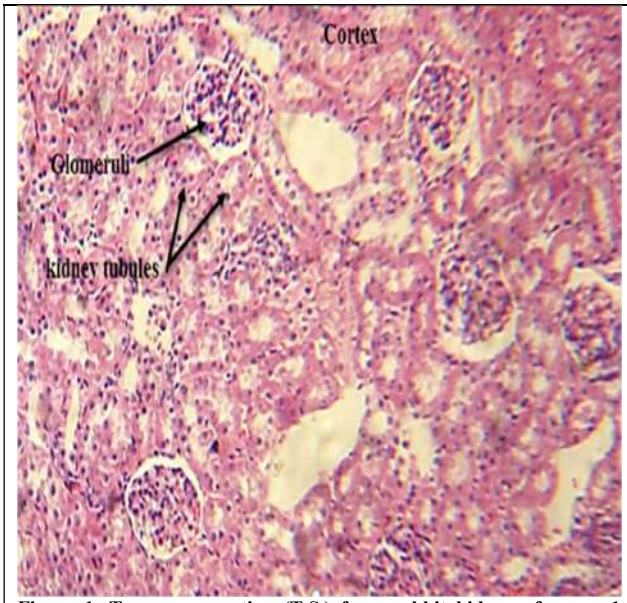

Figure 1. Transverse section (T.S.) from rabbit kidney of group 1 (control) treatment with physiological solution for 21 days shows: normal renal glomeruli and renal tubules (RT) (H&E Stain, 100X).

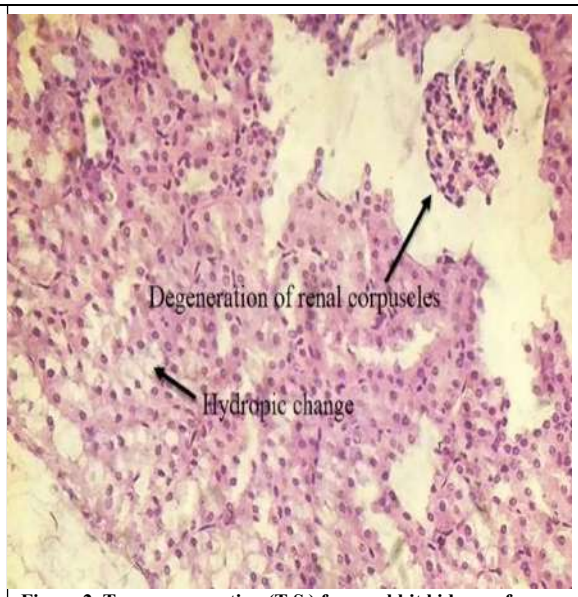

Figure 2. Transverse section (T.S.) from rabbit kidney, of group 2, treated with 66.5 mg/ kg-^{1}.body.weight/ day Cypermethrin for 21 day shows: Degeneration of Renal Corpuscles and Hydropic Change (H&E Stain, 100x)

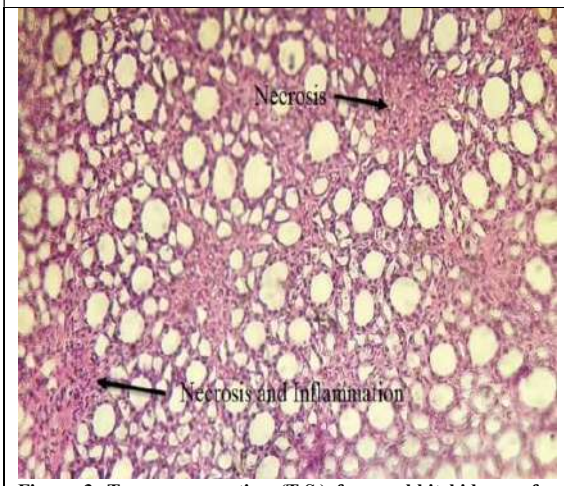

Figure 3. Transverse section (T.S.) from rabbit kidney, of group 2, treated with 66.5 mg/ kg-^{1}.body.weight/ day Cypermethrin for 21 day shows : Necrosis and Inflammation (H&E Stain, 100x) .

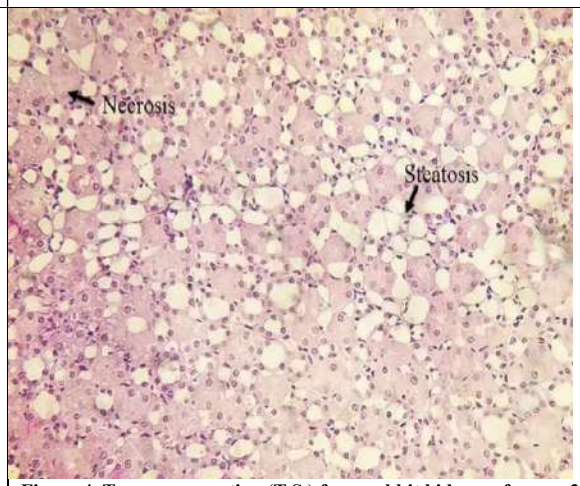

Figure 4. Transverse section (T.S.) from rabbit kidney, of group 2, treated with 66.5 mg/ kg-^{1}.body.weight/ day Cypermethrin for 21 day shows :Steatosis and Necrosis (H&E Stain, 100x)

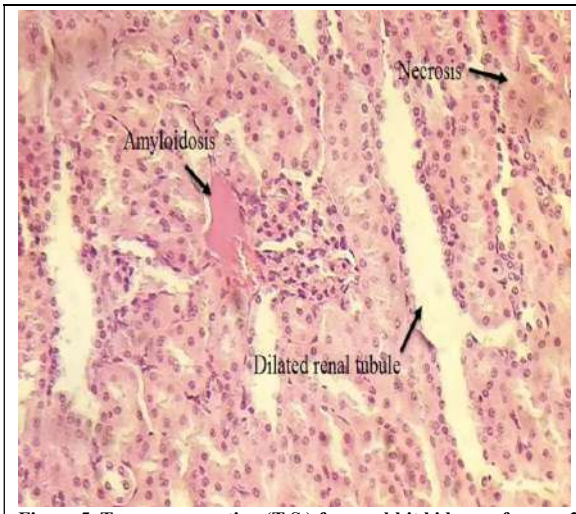

Figure 5. Transverse section (T.S.) from rabbit kidney, of group 2, treated with 66.5 mg/ kg-^{1}.body.weight/ day Cypermethrin for 21 day shows : Dilated Renal Tubule, Necrosis and amyloidosis (H&E Stain, 400x) .

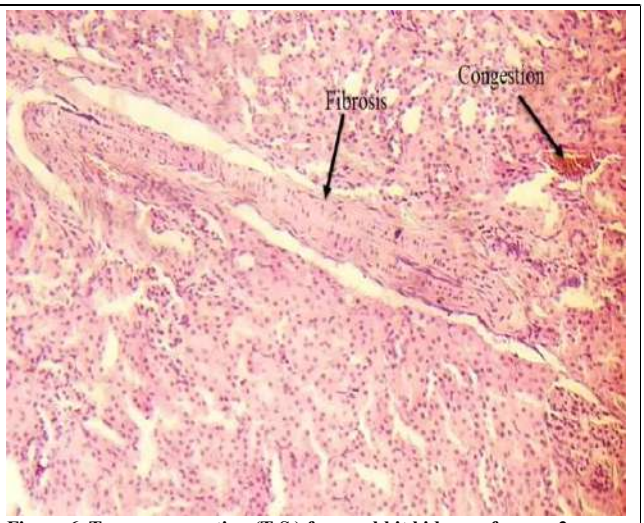

Figure 6. Transverse section (T.S.) from rabbit kidney, of group 2, treated with 66.5 mg/ kg-^{1}.body.weight/ day Cypermethrin for 21 day shows : Congestion and Fibrosis (H&E Stain, 400x) .

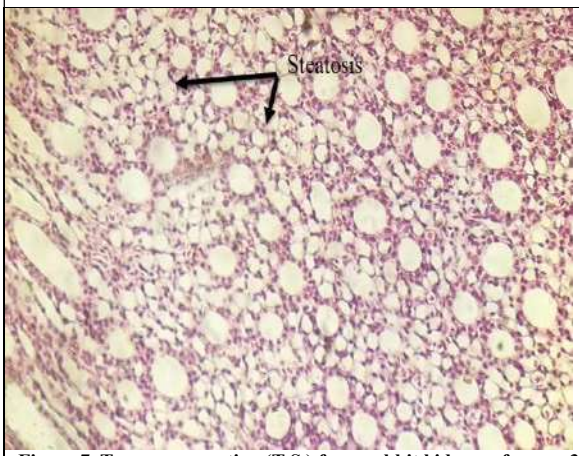

Figure 7. Transverse section (T.S.) from rabbit kidney, of group 3, treated with 133 mg/ kg-^{1}.body.weight/ day Cypermethrin for 21 day shows : Steatosis (H&E Stain, 100x).

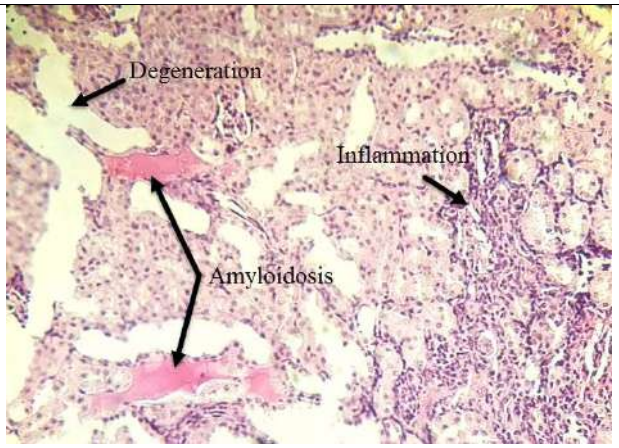

Figure 8. Transverse section (T.S.) from rabbit kidney, of group 3, treated with 133 mg/ kg-^{1}.body.weight/ day Cypermethrin for 21 day shows : Inflammation, Degeneration and Amyloidosis (H&E Stain, 400x).

DISCUSSION

The present investigation revealed marked histopathological alterations in renal tissues following cypermethrin exposure. These changes were consistent with the observations of Shuklan et al. (2023). Similar findings were reported by Manna et al. (2004) and Hussien et al. (2013), who noted that the lipophilic nature of cypermethrin enables its penetration through cellular membranes, resulting in structural damage and leakage of intracellular enzymes. Grewal et al. (2010) further demonstrated that cypermethrin intoxication disrupts renal architecture, leading to glomerular shrinkage, tubular necrosis, hemorrhage, and epithelial sloughing in the convoluted tubules. Elevated plasma levels of urea and creatinine, biomarkers of renal dysfunction, were also associated with these histopathological changes (Grewal et al., 2009).

Comparable toxic effects were observed in the cypermethrin-treated groups of the current study. Shivanoor and David (2014) reported that deltamethrin exposure caused proximal tubular dilation, inflammation, cellular infiltration, and necrosis due to epithelial desquamation. Likewise, Raj et al. (2013) documented medullary congestion in the kidneys of mice following oral administration of a cypermethrin–endosulfan combination. Faten and Abdulhadi (2016) also described extensive renal damage in albino rats, including Bowman's space dilation, tubular cell degeneration, glomerular atrophy, hemorrhage, epithelial sloughing, glomerulonephritis, tubular lining necrosis, eosinophilic material deposition, tubular destruction, inflammatory cell aggregation, disorganization of renal

architecture, glomerular destruction, and severe tubular necrosis.

The accumulation of cypermethrin in renal tissues likely contributes to these toxic manifestations. Prashanth (2011) suggested that the upregulation of metallothionein, a metal-binding protein, in response to cypermethrin exposure may impair organelle function within renal cells, thereby exacerbating tissue injury. Mamun et al. (2014) similarly reported that cypermethrin intoxication adversely affects kidney structure, causing glomerular shrinkage, tubular necrosis, hemorrhage, and epithelial sloughing. Once absorbed into the bloodstream, cypermethrin undergoes hepatic metabolism, producing reactive intermediates that bind to cellular macromolecules, inducing oxidative stress, lipid peroxidation, and subsequent cellular damage. Latif et al. (2011) observed renal lesions in cypermethrin-treated rabbits, including pyknotic nuclei, necrosis, epithelial sloughing, cast deposition, and increased urinary space.

Pyrethroids such as cypermethrin are known to induce oxidative stress by generating free radicals, which compromise the glomerular filtration barrier. This damage alters the negative charge of structural components—including endothelium, podocytes, and basement membrane—either neutralizing or reversing it, thereby increasing protein permeability. Degenerative changes in the kidneys result in detachment of epithelial cells from tubular basement membranes. These detached cells, together with leaked proteins, form epithelial casts within renal tubules (Khan et al., 2009).

Finally, the findings are corroborated by Kundu et al. (2026), who reported widespread inflammatory cell clusters, severe hypertensive glomerulosclerosis, and extensive tubular necrosis in the kidneys of cypermethrin-exposed mice. Additional pathological features included blackish glomerular discoloration, marked hemorrhage, and tubular enlargement. High-resolution histopathological imaging further revealed abnormal glomerular architecture and a significant reduction in viable cell counts in both hepatic and renal tissues of the treated group.

CONCLUSION

It could be concluded from this study that administration of cypermethrin caused significant histopathological changes in renal tissues of rabbits. Additionally, our results demonstrate that the nephrotoxicity intensity correlates with the increase in dose of cypermethrin administration.

RECOMMENDATIONS

Further research is required to clarify the molecular and cellular mechanisms underlying cypermethrin-induced nephrotoxicity. Regulatory measures limiting the use of cypermethrin in agricultural and veterinary practices should be considered to reduce human and animal exposure. In addition, systematic monitoring of cypermethrin residues in the environment and food supply is essential for evaluating potential long-term health risks.

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CONTRIBUTORS OF UTHORS

AMJ. Al-Arami and A AY Al-Rezaki have equally contributed in the designing, carried out, writing the first draft and final of the manuscript. Both authors have reviewed and approved the last submitted version.

COMPETING INTERESTS

Authors declare that there is no conflict of interest.

ETHICS APPROVAL

This study was performed in line with National Institutes of Health(NIH) guidelines for the care and use of laboratory animals, and approved by the Institutional Ethics Committee at the Faculty of education, Thamar University.

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None.

DATA AVAILABILITY STATEMENT

The data are available within the article.

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السمية الكلوية الناجمة عن السايبرميثرين في الأرانب: دراسة نسيجية مرضية

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الملخص

تم تصميم هذه الدراسة للتحقق من التغيرات النسيجية في كلى الأرانب بعد التعرض لمبيد السيبرمثرين، وهو أحد مبيدات البيرثرويد من النوع الثاني، ويُستخدم على نطاق واسع لحماية المحاصيل من الآفات والحشرات، لكنه يرتبط أيضًا بالتلوث البيئي والمخاطر الصحية. استخدم في الدراسة 18 أرنبًا ذكرًا بالغًا، وتم تقسيمها عشوائيًا إلى ثلاث مجموعات، تضم كل مجموعة ستة حيوانات. المجموعة الأولى كانت مجموعة ضابطة وتلقت محلول ملحي طبيعي يوميًا. المجموعة الثانية أعطيت السيبرمثرين عن طريق الفم بجرعة تعادل 10/1 من الجرعة المميتة النصفية (66.5 ملغ/كغ من وزن الجسم) مرة يوميًا لمدة 21 يومًا متتاليًا. أما المجموعة الثالثة فقد تلقت جرعة أعلى تعادل 5/1 من الجرعة المميتة النصفية (133 ملغ/كغ من وزن الجسم) بنفس الجدول الزمني. أظهر الفحص النسيجي للمجموعات المعالجة تغيرات مرضية متعددة مقارنة بالمجموعة الضابطة؛ حيث تسبب السيبرمثرين في تنكس الكبيبات الكلوية، تغيرات مائية، نخر، التهابات، تنكس دهني، داء النشواني، توسع الأنابيب الكلوية، احتقان، توليف، دهن كبدي، وتنكس أنبوبي. **خلصت الدراسة الى ان** السيبرمثرين أحدث أضرارًا نسيجية كبيرة في كلى الأرانب التي خضعت للدراسة. ينبغي أجراء دراسات اضافية لتوضيح الآليات الجزيئية والخلوية للسمية الكلوية الناجمة عن السايبرمثرين.

الكلمات المفتاحية: السيبرميثرين، التغيرات النسيجية المرضية، الكلى، السمية، الأرانب.

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