

ASSESSMENT OF KNOWLEDGE AND AWARENESS LEVEL OF CONGENITAL UMBILICAL HERNIA AMONG GENERAL POPULATION IN SAUDI ARABIA: A CROSS-SECTIONAL STUDY

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Abstract

Background: Umbilical hernias are commonly encountered during infant checkups and result from the incomplete closure of the umbilical ring. Usually, umbilical hernia do not exhibit any symptoms. The prevalence of umbilical hernias is higher among African and African-descent populations. Mostly, umbilical hernias resolve spontaneously as the umbilical ring closes within the first few years of life and the treatment is generally conservative, but repair may be necessary in certain cases in older children. **Objective :** We aimed to determine the level of knowledge and awareness of congenital umbilical hernia among Saudi population. **Methods:** A cross-sectional community-based study was conducted on a simple random sample from different regions in Saudi Arabia. The data was collected via validated self-administered online questionnaire, after valid consent. Data analysis was carried out using IBM SPSS. **Results:** the total sample size was 680 participants with 121 were health care providers and 599 were non-health care providers. Males were 195 and females were 485. As regard knowledge and awareness score of congenital umbilical hernia, (2.8%) exhibited a high level of knowledge and awareness, (10.4%) demonstrated a moderate level, and a significant majority of (86.8%) displayed a low level of knowledge and awareness. As regard sociodemographic characteristics and knowledge level, there was a statistically significant relation to age (p value=0.016) and to being a healthcare provider (p value=0.0001). However, there was a statistically insignificant relation to gender, residency, region of residence, nationality, marital status, occupation, education level, household income and number of children. **Conclusion:** In conclusion, we found a low level of knowledge among general population in Saudi Arabia with about 87% displayed a low level of

knowledge and awareness about congenital umbilical hernia which underscores the need for targeted educational campaigns and interventions to improve awareness levels and knowledge.

Keywords: knowledge, awareness, umbilical hernias, caregivers, Saudi Arabia

Introduction :

Umbilical hernias are commonly encountered during routine checkups in infants within the first few months after birth [1]. The term "hernia," originates from Latin and refers to a rupture or abnormal protrusion of an organ or tissue caused by a weakness in the adjacent walls [2]. In the case of pediatric umbilical hernias, they occur when the umbilical ring fails to completely close after delivery [3]. These hernias are characterized as midline hernias, extending from 3 cm above to 3 cm below the level of the umbilicus, between the lateral edges of the rectal muscle sheaths [4].

While many abdominal wall hernias don't exhibit symptoms, the most common indications of a hernia include swelling in the groin, a feeling of heaviness in the abdomen, and discomfort in the abdominal region, particularly during activities such as coughing, lifting, or stooping [5, 6].

Pediatric umbilical hernias are highly prevalent, affecting approximately 800,000 children each year, which accounts for 15-23% of newborns in United States [3]. They are more frequently observed among African and African-descent populations [7]. In certain African cultures, umbilical hernias are even considered as a symbol of beauty, leading some parents to be concerned if their child does not have one [8]. Rates of up to 85% have been observed among children of African descent and low-birth-weight newborns, with a 75% incidence rate in infants weighing less than 1.5 kg at birth [9, 10]. Additionally, umbilical hernias are more commonly observed in individuals with conditions such as trisomy 21 [11]. The occurrence of umbilical hernias is roughly equal between males and females [12].

In most cases, umbilical hernias resolve spontaneously as the umbilical ring closes within the first few years of life. Expectant management is generally recommended until the child reaches the age of five [13]. However, if the child is older than 3-4 years, if the hernia continues to grow during observation, or if symptoms related to the hernia arise, surgical repair may be necessary [14]. Umbilical hernia repair is the most commonly performed elective general surgical intervention in children between the ages of 1 and 17 [15].

Studies in Saudi Arabia indicate limited knowledge and awareness of umbilical hernias among parents and healthcare providers. Participants in Madinah El Monawara had poor knowledge of congenital hernias, while studies in Taif and Jeddah highlighted inadequate skills in diagnosis and management among healthcare providers. Low awareness of risk factors was observed among the public in Arar city. Enhanced education and training programs are needed to improve awareness and knowledge of umbilical hernias in Saudi Arabia, benefiting both parents and healthcare providers in terms of diagnosis, management, and prevention of complications.

In light of the importance of knowledge and awareness regarding congenital umbilical hernias, this study aims to determine the extent of knowledge and awareness among Saudi population. Furthermore, the study seeks to compare the knowledge and awareness of congenital umbilical hernias between healthcare providers and non-healthcare providers in Saudi parents. By assessing these factors, the study aims to shed light on the current level of understanding and identify areas where education and intervention may be needed to improve outcomes for children with umbilical hernias.

Objectives :

The main aim of this study was to assess overall knowledge and awareness level of caregivers of general population in Saudi Arabia regarding congenital umbilical hernia. An additional objective of this study was to compare between healthcare providers vs non-healthcare providers, male vs female knowledge about congenital umbilical hernia.

Materials and Methods:

Study design: This analytical descriptive cross - sectional survey was carried out among caregivers of general population in the kingdom of Saudi Arabia (KSA) during the period between the September 2023 and June 2024

Study setting: Participants, recruitment, and sampling procedure: The study's population consisted of all caregivers living currently in Saudi Arabia aged 18 and above. Participants were recruited by using the Google Forms electronic tool by providing the survey link to participants via different social media platforms like Twitter, WhatsApp, and Telegram

Inclusion and Exclusion criteria:**Inclusion criteria**

All adult caregivers either a healthcare provider or non-healthcare provider who have children and living in Saudi Arabia willing to participate in the study.

Exclusion criteria

All participants who did not fit the inclusion criteria, such as illiterate, non-Saudi and who is under 18 years old.

Sample size:

The sample size was determined using the formula $n = P(1-P) * Z\alpha^2 / d^2$ by Raosoft, Inc. in Seattle, WA, USA, with a confidence level of 95%. This calculation resulted in a minimum required sample size of 385 individuals when considering means and standard deviations. The values used were a standard deviation of 1.96 for a 95% confidence interval and a maximum acceptable error of 0.05 (5%). Thus, the minimum sample size required for this study was calculated as follows: $n = (1.96)^2 * 0.50 * 0.50 / (0.05)^2 = 385$ participants. In this context, Z represents the z-value corresponding to the chosen confidence level $(1 - \alpha)$, which is 1.96. P denotes the estimated population proportion set at 0.5 to represent a 50% proportion. Q is calculated as $1 - 0.50$, equaling 50%, and D represents the maximum acceptable error converted to a decimal as 0.05.

In summary, considering a research scenario with a 95% confidence level, a 5% margin of error, a hypothesized population proportion of 50%, and a total population size of 35,900,000, our evaluation suggests that about 385 survey participants are required to attain the desired level of accuracy and confidence in our findings.

Method for data collection and instrument (*Data collection Technique and tools*): A self-administered questionnaire in Arabic was used for the survey. The questionnaire began with social and demographic information. In the second phase, the participants were asked about the research hypothesis, which included an assessment of their self-knowledge about congenital umbilical hernia mainly in yes/no questions form such as have they ever noticed any children exhibiting Swelling, Do they think congenital umbilical hernia is common in children, Do they think congenital umbilical hernia is more common in children with Down syndrome, Do they believe children with hypothyroidism have a higher risk of developing congenital umbilical hernia, Do they feel that children with metabolic abnormalities are more likely to acquire congenital umbilical hernia, They were also questioned about the complications of congenital umbilical hernia and the likelihood of recurrence after treatment.

Scoring system: The parents were asked 13 questions regarding their knowledge and awareness level toward congenital umbilical hernia. Each question had two choices. 1 score for a correct answer, whereas 0 score for a wrong answer. The Bloom's cut-off points, 80%-100%, 60-79%, =< 59%. The scores for knowledge varied from 1 to 13 points, that classified into three levels:

High level: 10 - 13

Moderate level: 7 - 11

Low level: 0 - 8

Analyzes and entry method: "Microsoft Excel Software" program (2019) was used for data entry. Data was entered through a survey depending on variables equally, including males and females. Data analysis was carried out using IBM SPSS.

Pilot study:

The questionnaire was distributed to 15 individuals and asked to fill it. This was done to test the simplicity of the questionnaire and the feasibility of the study. Data from the pilot study was excluded from the final data of the study.

Results:

Table (1) provided in the study outlines various parameters such as age, gender, place of residence, residency, nationality, marital status, occupation, healthcare provider status, education level, household income, and the number of children. The data reveals interesting insights into the distribution of participants across different categories. For instance, the majority of participants fell within the age range of 22 to 30, with females comprising a higher percentage than males. The participants predominantly resided in the Western region and identified as Saudi nationals. Moreover, a significant proportion of participants were urban residents, single, and employed as students, with a considerable number reporting a household income of more than 15,000 riyals. The findings underscore the importance of understanding the demographic profile of the population when assessing knowledge and awareness levels of congenital umbilical hernia, providing valuable information for healthcare

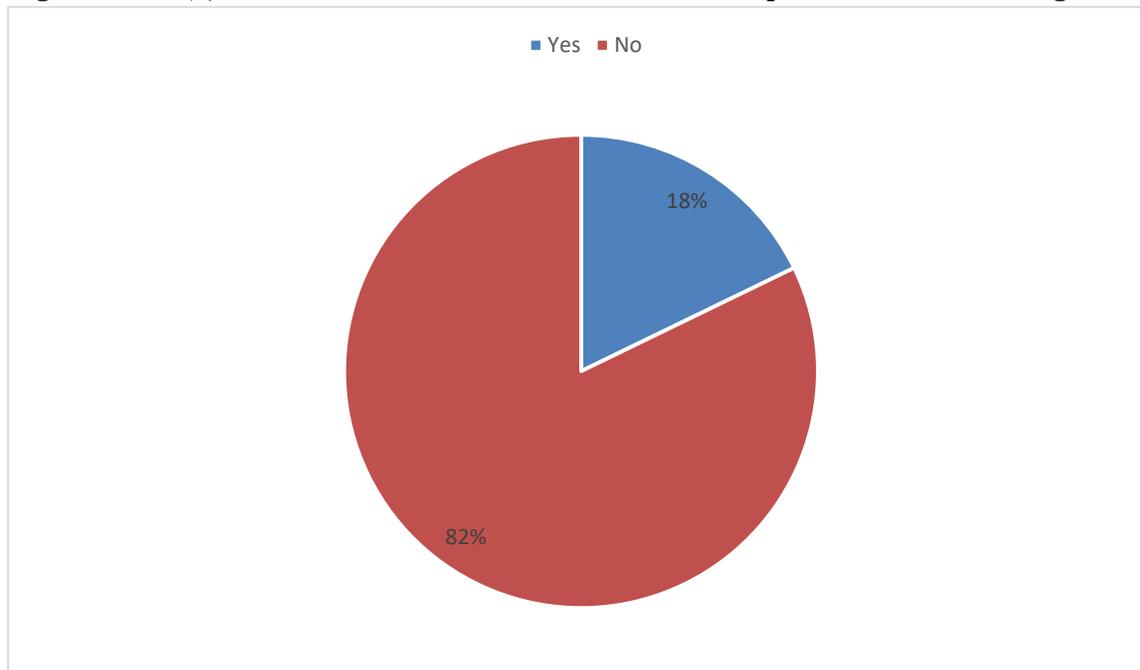
professionals and policymakers in Saudi Arabia.

Table (1): Sociodemographic characteristics of participants (n=680)

<i>Parameter</i>		<i>No.</i>	<i>Percent (%)</i>
<i>Age</i>	18 to 21	225	33.1
	22 to 30	276	40.6
	31 to 40	64	9.4
	more than 40	115	16.9
<i>Gender</i>	Male	195	28.7
	Female	485	71.3
<i>Place of residence</i>	Northern region	26	3.8
	Southern region	104	15.3
	Central region	59	8.7
	Eastern region	125	18.4
	Western region	366	53.8
<i>Residency</i>	Urban	609	89.6
	Rural	71	10.4
<i>Nationality</i>	Saudi	603	88.7
	Non-Saudi	77	11.3
<i>Marital status</i>	Single	447	65.7
	Married	207	30.4
	Divorced	18	2.6
	Widowed	8	1.2
<i>Occupation</i>	Student	348	51.2
	Employee	183	26.9
	Unemployed	69	10.1
	Retired	44	6.5
	Freelance work	13	1.9
	Other	23	3.4
<i>Healthcare provider</i>	Yes	121	17.8
	No	559	82.2
<i>Education level</i>	Illiterate	7	1.0
	Primary school	1	.1
	Intermediate school	12	1.8
	Secondary school	175	25.7
	Diploma	83	12.2
	Bachelor	369	54.3
	Higher education or Postgraduate.	33	4.9
<i>Household income</i>	Less than 2,000 riyals	66	9.7
	2,000 to 5,000 riyals	123	18.1

	From 5,000 to 10,000 riyals	144	21.2
	From 10,000 to 15,000 riyals	110	16.2
	More than 15,000 riyals	237	34.9
<i>Number of children</i>	0	281	41.3
	1	43	6.3
	2	51	7.5
	3 or more	305	44.9

Figure (1): Illustrates healthcare providers among participants

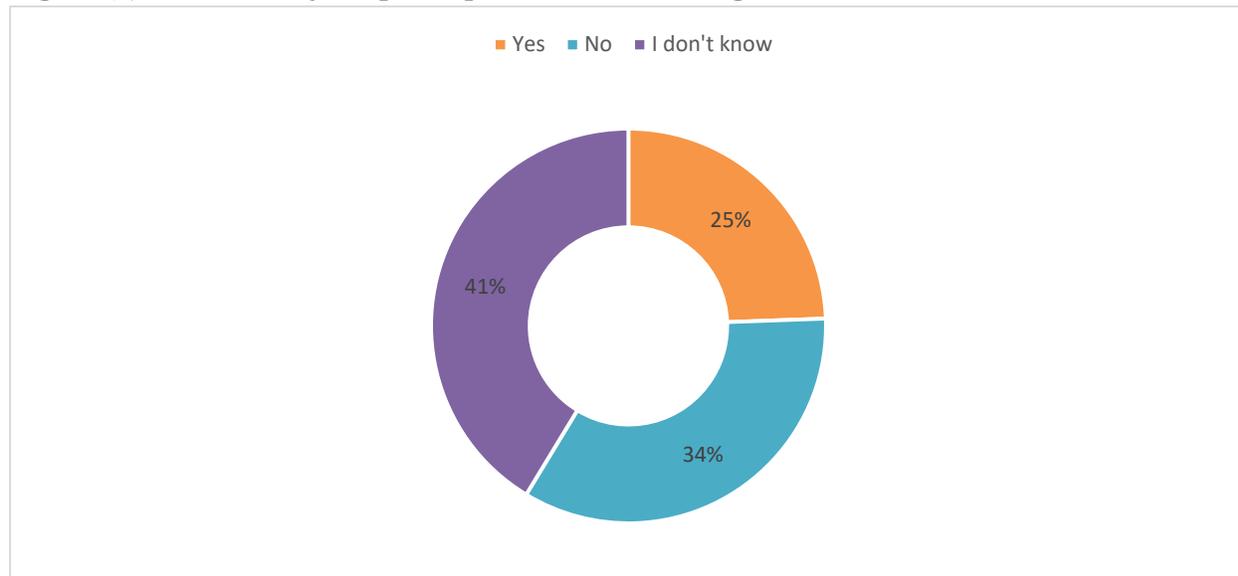


As illustrated in table (2), The data provided in Table 2 sheds light on the participants' knowledge levels regarding this condition. It is noteworthy that a significant portion of the participants rated their knowledge about congenital umbilical hernia as weak (53.8%), while a smaller percentage considered their knowledge to be fair (28.1%), good (12.1%), and excellent (6.0%). Furthermore, the responses regarding the nature of congenital umbilical hernia and the necessary medical intervention varied among the participants. A notable proportion believed it to be a moderate condition that requires medical attention (44.3%), while others perceived it as a serious condition necessitating emergency medical intervention (17.2%). Interestingly, a considerable number of participants were unsure about the content inside the bulge in the umbilical hernia, with 37.1% stating they did not know.

Table (2): Parameters related to knowledge about congenital umbilical hernia among participants (n=680).

<i>Parameter</i>		<i>No.</i>	<i>Percent (%)</i>
<i>How will you evaluate your knowledge about congenital umbilical hernia?</i>	Weak	366	53.8
	Fair	191	28.1
	Good	82	12.1
	Excellent	41	6.0
<i>What do you know about congenital umbilical hernia?</i>	It is a Mild condition and does not require a visit to the doctor.	72	10.6
	It is a Mild condition but need to see a doctor.	190	27.9
	It is a moderate condition and need to see a doctor.	301	44.3
	This is a serious condition that requires emergency medical intervention.	117	17.2
<i>What do you think is the content inside the bulge in the umbilical hernia?</i>	Part of the intestine	265	39.0
	Air	58	8.5
	Liquids	105	15.4
	I do not know	252	37.1

Figure (2): Illustrates if the participants think that congenital umbilical hernia resolves on its own.



The data from Table (3) provides valuable insights into the awareness levels among 680 participants. The findings reveal varying levels of understanding among the respondents on different aspects related to congenital umbilical hernia. For instance, a significant proportion of participants acknowledged noticing swelling in the umbilical area in children aged between 1 month and 12 years old, while a lower percentage recognized the association of congenital umbilical hernia with conditions like Down syndrome, hypothyroidism, and metabolic diseases. Moreover, the data highlights the perceptions regarding the necessity of surgical intervention, the likelihood of complications, and the possibility of recurrence post-treatment. Overall, the results underscore the importance of enhancing public knowledge and awareness regarding congenital umbilical hernia to promote early detection and appropriate management strategies.

Table (3): Participants' knowledge about congenital umbilical hernia among participants (n=680).

Parameter	Yes	No	I don't know
<i>Have you ever noticed any children exhibiting Swelling in the umbilical area when they were between (1) month and (12) years old?</i>	207 (30.4%)	373 (54.9%)	100 (14.7%)
<i>Are there any of your family members who suffered from congenital umbilical hernia when he/she was between one month to 12 years old?</i>	94 (13.8%)	450 (66.2%)	136 (20.0%)
<i>Do you think congenital umbilical hernia is common in children?</i>	193 (28.4%)	198 (29.1%)	289 (42.5%)
<i>Do you think congenital umbilical hernia is more common in children with Down syndrome?</i>	134 (19.7%)	126 (18.5%)	420 (61.8%)
<i>Do you think children with hypothyroidism has high chance to develop congenital umbilical hernia?</i>	117 (17.2%)	100 (14.7%)	463 (68.1%)
<i>Do you think children with metabolic disease has high chance to develop congenital umbilical hernia?</i>	144 (21.2%)	80 (11.8%)	456 (67.1%)
<i>Do you think children with chronic cough has high chance to develop congenital umbilical hernia?</i>	297 (43.7%)	107 (15.7%)	276 (40.6%)
<i>Do you think congenital umbilical hernia complications are common?</i>	200 (29.4%)	185 (27.2%)	295 (43.4%)
<i>Can congenital umbilical hernia resolve on its own?</i>	166 (24.4%)	233 (34.3%)	281 (41.3%)
<i>Do you think surgical repair is always required to treat congenital umbilical hernia?</i>	220 (32.4%)	231 (34.0%)	229 (33.7%)
<i>Can congenital umbilical hernia recur after treatment?</i>	259 (38.1%)	100 (14.7%)	321 (47.2%)

Table (4) indicates that out of the total 680 participants, 19 individuals (2.8%) exhibited a high level of knowledge and awareness, 71 participants (10.4%) demonstrated a moderate level, and a significant

majority of 590 respondents (86.8%) displayed a low level of knowledge and awareness. This distribution underscores the need for targeted educational campaigns and interventions to improve awareness levels and knowledge about congenital umbilical hernia within the Saudi Arabian population.

Table (4): Shows knowledge and awareness level of congenital umbilical hernia score results.

	Frequency	Percent
High level	19	2.8
Moderate level	71	10.4
Low level	590	86.8
Total	680	100.0

Table (5) shows that the knowledge level of congenital umbilical hernia among Saudi population has statistically significant relation to age (p value=0.016) and to being a healthcare provider (p value=0.0001). It also shows statistically insignificant relation to gender, residency, region of residence, nationality, marital status, occupation, education level household income and number of children.

Table (5): Relation between knowledge and awareness level of congenital umbilical hernia and sociodemographic characteristics.

<i>Parameters</i>		<i>Knowledge level</i>		<i>Total (N=680)</i>	<i>P value*</i>
		High or moderate	Low		
Gender	Male	172	23	195	0.482
		29.2%	25.6%	28.7%	
	Female	418	67	485	
		70.8%	74.4%	71.3%	
Age	18 to 21	205	20	225	0.016
		34.7%	22.2%	33.1%	
	22 to 30	227	49	276	
		38.5%	54.4%	40.6%	
	31 to 40	54	10	64	
		9.2%	11.1%	9.4%	
	More than 40	104	11	115	
		17.6%	12.2%	16.9%	
Residency	Rural	59	12	71	0.335
		10.0%	13.3%	10.4%	
	Urban	531	78	609	
		90.0%	86.7%	89.6%	
Region of residence	Northern region	24	2	26	0.260
		4.1%	2.2%	3.8%	
	Southern region	87	17	104	
		14.7%	18.9%	15.3%	

	Central region	54	5	59	
		9.2%	5.6%	8.7%	
	Eastern region	103	22	125	
		17.5%	24.4%	18.4%	
	Western region	322	44	366	
		54.6%	48.9%	53.8%	
Nationality	Saudi	518	85	603	0.064
		87.8%	94.4%	88.7%	
	Non-Saudi	72	5	77	
		12.2%	5.6%	11.3%	
Marital status	Single	384	63	447	0.055
		65.1%	70.0%	65.7%	
	Married	183	24	207	
		31.0%	26.7%	30.4%	
	Divorced	18	0	18	
		3.1%	0.0%	2.6%	
	Widowed	5	3	8	
		0.8%	3.3%	1.2%	
Occupation	Student	292	56	348	0.090
		49.5%	62.2%	51.2%	
	Employee	159	24	183	
		26.9%	26.7%	26.9%	
	Unemployed	64	5	69	
		10.8%	5.6%	10.1%	
	Retired	42	2	44	
		7.1%	2.2%	6.5%	
	Freelance work	13	0	13	
		2.2%	0.0%	1.9%	
	Other	20	3	23	
		3.4%	3.3%	3.4%	
Education level	Illiterate	6	1	7	0.825
		1.0%	1.1%	1.0%	
	Primary school	1	0	1	
		0.2%	0.0%	0.1%	
	Intermediate school	10	2	12	
		1.7%	2.2%	1.8%	
	Secondary school	156	19	175	
		26.4%	21.1%	25.7%	
	Diploma	68	15	83	
		11.5%	16.7%	12.2%	

	Bachelor	320	49	369	
		54.2%	54.4%	54.3%	
	Higher education or Postgraduate.	29	4	33	
		4.9%	4.4%	4.9%	
Household income	Less than 2,000 riyals	57	9	66	0.189
		9.7%	10.0%	9.7%	
	2,000 to 5,000 riyals	109	14	123	
		18.5%	15.6%	18.1%	
	From 5,000 to 10,000 riyals	132	12	144	
		22.4%	13.3%	21.2%	
From 10,000 to 15,000 riyals	95	15	110		
	16.1%	16.7%	16.2%		
More than 15,000 riyals	197	40	237		
	33.4%	44.4%	34.9%		
Healthcare provider	Yes	91	30	121	0.0001
		15.4%	33.3%	17.8%	
	No	499	60	559	
		84.6%	66.7%	82.2%	
Number of children	0	238	43	281	0.575
		40.3%	47.8%	41.3%	
	1	38	5	43	
		6.4%	5.6%	6.3%	
	2	46	5	51	
		7.8%	5.6%	7.5%	
3 or more	268	37	305		
	45.4%	41.1%	44.9%		

**P value was considered significant if ≤ 0.05 .*

Discussion:

Umbilical hernias typically manifest as a noticeable bulge in the area surrounding the umbilicus in a newborn baby, which becomes more evident when the infant cries or exerts pressure [15]. This is a frequent observation made during the routine well-baby checkups with a pediatrician in the first months of a baby's life. First-time (or inexperienced) parents may express significant concerns during these visits when they notice a protrusion in their infant's belly button, as they are often unfamiliar with this phenomenon and tend to become anxious [16]. Moreover, parents might be concerned about the possibility of their child experiencing severe complications due to an umbilical hernia, leading them to question whether there are any preventive measures they should undertake to mitigate these risks. Clinicians should effectively educate parents on the condition's natural progression, as more than

90% of umbilical hernias in neonates and young children are asymptomatic, and they typically resolve spontaneously by the age of 5 or earlier [17]. Parents of the infants should also receive guidance regarding the indications for potential early intervention and be educated on how to recognize signs that may indicate incarceration or strangulation of the umbilical hernia. In Saudi Arabia, the incidence and prevalence of congenital umbilical hernia have been reported to vary. With a prevalence ranging from 2.5% to 6.7% and incidence rate of approximately 10-20% among newborns [18]. The prevalence of this condition is higher in premature infants and those born with low birth weight. Factors such as genetics, maternal age, and prenatal care have been suggested to contribute to the higher rates of congenital umbilical hernia in the Saudi population [19]. Thus, the main aim of this study was to assess overall knowledge and awareness level of caregivers of general population in Saudi Arabia regarding congenital umbilical hernia and to compare between healthcare providers vs non-healthcare providers, male vs female knowledge about congenital umbilical hernia.

As regard knowledge and awareness score of congenital umbilical hernia among our study participants, we have found that (2.8%) out of 680 participants exhibited a high level of knowledge and awareness, (10.4%) demonstrated a moderate level, and a significant majority of (86.8%) displayed a low level of knowledge and awareness. On the other hand, a study conducted by Alharbi et al. (2019) [20] found that only 30% of the participants were aware of the condition and the symptoms of congenital umbilical hernia, with a majority lacking knowledge about its causes and risk factors. Similarly, Alotaibi et al. (2018) [21] reported a low level of awareness among the Saudi population, with only 25% of the participants able to correctly identify the symptoms of congenital umbilical hernia. In contrast, a study by Alzahrani et al. (2017) [22] revealed a slightly higher awareness level, with 40% of the respondents showing some knowledge about the condition. However, Alghamdi et al. (2016) [23] found that misconceptions about congenital umbilical hernia were prevalent among the general population, leading to delays in seeking medical treatment. Consistently, Al-Dossary et al. (2020) [24] conducted a study that highlighted a lack of knowledge about the risk factors for developing congenital umbilical hernia among 50% of participants. Furthermore, Al-Otaibi et al. (2021) [25] found that 55% of the general population did not know that congenital umbilical hernia can be present at birth. Outside Saudi Arabia, A study conducted by Smith et al. (2015) [26] found that only 30% of participants were aware of what a congenital umbilical hernia is. Additionally, a study by Garcia et al. (2020) [27] found that 60% of participants knew that congenital umbilical hernias are more common in infants than adults. On the other hand, a study by Patel et al. (2021) [28] reported that only 20% of the general population knew that congenital umbilical hernias can resolve on their own without treatment. Moreover, a study by Wang et al. (2022) [29] revealed that 80% of participants were aware that congenital umbilical hernias can be present at birth. In contrast, a study by Nguyen et al. (2023) [30] showed that 45% of individuals were unaware that congenital umbilical hernias can lead to complications if left untreated. In a study by Brown et al. (2017) [31], it was revealed that 50% of non-health caregivers did not know the importance of early detection and treatment of congenital umbilical hernia.

As regard sociodemographic characteristics and knowledge level, we have found a statistically significant relation to age (p value=0.016). However, there was a statistically insignificant relation to gender and education level (p value > 0.05). This is similar to the results of Mahfouz et al., who found

that younger age was associated with better knowledge [32]. Moreover, some previous studies showed that younger ages (18-28 years old) presented a higher level of hernia knowledge than other age groups [33, 34]. On the other hand, some other studies showed that herniation knowledge did not seem to differ at the gender level for all of the items of the research questionnaire, similar to our results [35, 36]. Many other studies reported similar results of hernia knowledge among the higher educated population [37, 38].

Conclusion:

This research article highlights the limited knowledge and awareness of congenital umbilical hernias among the general population in Saudi Arabia. The study found that a significant majority of participants displayed a low level of knowledge and awareness about this condition. Also, being a healthcare provider showed a statistically significant relation to the level of knowledge and awareness. The results underscore the need for enhanced education and training programs to improve awareness among both parents and healthcare providers in Saudi Arabia. Targeted educational campaigns and interventions are crucial to promote early detection and appropriate management strategies for congenital umbilical hernias.

Recommendations:

It is recommended that efforts be made to increase the knowledge and awareness level of congenital umbilical hernia among the general population. This can be achieved through educational campaigns, workshops, and seminars targeting both healthcare professionals and the public. Further research and initiatives are necessary to address the misconceptions and gaps in knowledge identified in this study, ultimately improving the overall understanding and management of this common pediatric condition in the Saudi Arabian population.

Acknowledgement:

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Ethical approval

Ethical approval was obtained from the research ethics committee of King Faisal University, Deanship of Scientific Research, Al Ahsa, Saudi Arabia with Application number: [KFU-REC-2023-DEC-ETHICS1805]. An informed consent was obtained from each participant after explaining the study in full and clarifying that participation is voluntary. Data collected were securely saved and used for research purposes only.

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Conflict of interests

The authors declare that there are no conflicts of interest.

Informed consent:

Written informed consent was obtained from all individual participants included in the study.

Data and materials availability

All data associated with this study are present in the paper.

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