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New insight into risk factors for gastroesophageal reflux in infants

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***Abstract*---**Background: Gastroesophageal reflux is a common problem in infancy. This study aimed to discover new risk factors that may contribute to gastroesophageal reflux in infants. Method and Materials: The current study adopted a case-control design to accomplish the objectives of the study for the period from 29th of December 2021 to 30th of June 2022. A probability sample was selected according to a systematic method for choosing the primary health care centers. A non-probability sample was purposively selected according to the inclusion and exclusion criteria of infants diagnosed with gastroesophageal reflux including a total of 140 infants aged from one month to twelve months, 70 infants with gastroesophageal reflux were in the study group and 70 infants in the healthy control group. Questionnaire form was applied to all participants at six enrolled primary health care centers in Mosul city. Results: The following studied hypothesized risk factors significantly differed between infants with gastroesophageal reflux and the healthy control group: twin infants (p=0.004), use of a pacifier (p=0.00), use of wrapping (p=0.00), exposure to smoking (p=0.00), family history of asthma (p=0.00), and starting position for infants (p=0.00). Conclusions: Throughout the course of the current study, a number of potential risk variables have been identified. These risk factors include having a twin, using wrapping, being exposed to smoking, having a family history of asthma, using pacifiers, and starting setting position for newborns. Recommendations include keeping infants away from smoking environments and avoiding the use of restrictive wrapping.

***Keywords*---**gastroesophageal reflux, risk factors, infants.

Introduction

Gastroesophageal reflux (GER) is the passage of gastric content into the esophagus with or without vomiting or regurgitation, the latter differs from vomiting because it is done without effort and does not present explosively, although sometimes in infants it can be very intense [1-3]. GER is a physiological phenomenon that occurs at all ages but mainly in infants. Regurgitation occurs daily in 50% of infants under three months of age and usually resolves spontaneously in most healthy infants by 12 to 18 months of age [4].

Factors unique to infants include anatomic factors, position, feeding methods, inflammation, anomalies, immaturity, and esophageal clearance mechanisms [5-7]. This study aimed to determine new risk factors that may play a role in gastroesophageal reflux in infants.

Design and period

The current study adopted a case-control design to accomplish the objectives of the study for the period from 29th of December 2021 to 30th of June 2022 at six enrolled primary health care centers in Mosul city.

Sample and Sampling

A non-probability sample was purposively selected according to the inclusion and exclusion criteria of infants diagnosed with gastroesophageal reflux who attended Mosul primary health care centers. A total number of (140) mothers of infants diagnosed with gastroesophageal reflux were interviewed to answer questions included in the questionnaire form.

Study Setting

The present study was conducted in Mosul city in Nineveh Governorate. It is a governorate in northern Iraq, with Mosul as its capital. Mosul is Iraq's second-largest city, located 465 kilometers north of Baghdad. Six primary health care centers were planned to be enrolled in this study; three canters from each side of the city bank. Primary health care centers were selected according to a systematic method. First, they were arranged according to the catchment area in descending order from the highest catchment area to the least number of catchment areas [8]. Then as we planned to take six PHC; so every PHC at each six centres intervals were enrolled thus choosing PHC number 1, 7 and 13 from each city bank; by choosing the first canter according to the catchment area, then omitting sex primary health centres and choose the 7th PHC, then ignoring another sex PHC and select the PHC with a rank of 13th. The primary health care centres selected according to this systematic method were (Saleh Al Shabkhoon Health Centre which has a population size in the catchment area of (66673), Al-Zanjeli Health Center (40342) and AL Rabee health center (23826) in the right bank of the city) (Al Aqsa health center (99260), Al Sharqi health center(66310) and Al qudis health center (40079) in

the left bank of the city) these Centers are located in the east and west of the Tigris River of Mosul city[9].

Study Tool

The instruments of the study were a structured interviewing questionnaire, which is composed of (5) parts, in which data were collected by personal interview, and included the following:

Part One: Sociodemographic characteristics of enrolled infants which include (birth date of infant, infant's age in months, Gender, ranking of an infant in the family.

Part two: the nutritional part which includes (the type of milk feeding, the age for starting complementary feeding (in months), inquires about infant allergy for cow milk protein, family allergy for cow milk protein food allergy, family allergy for any food item, pacifier use).

Part three: gastroesophageal reflux part: including (frequency of reflux per day, family history of reflux, type of delivery, use of wrapping, passive smoking, family history of asthma, family history of skin allergy, age to start setting position and position for infant's sleep).

Part four: The socioeconomic the family according to Scoring for modified Kuppuswamy's socioeconomic status scale.

Part five: Growth parameters of an infant including, weight, stature, OFC, and BMI; with their related percentiles.

Validity, reliability, and pilot study

The face and content validity of the study instrument was determined initially through a panel of (18) experts from different related specialties and from different institutions. The experts were asked to review and give their opinions about the contents of the instrument's application items of the study and its adequacy. The expert's responses were evaluated based on their agreements or disagreements and modifications had been done on each part and items of the guide implementation and its measurement, their mean of experience year was (27.45) years with a standard deviation (5.75).

In order to determine the reliability of parameters measurement in gastroesophageal reflux infants to measure the error in the measurement technique; therefore, each instrument used in the current study was assessed by statistical analysis. Correlation coefficients were computed to measure the reliability of the study tools, which was of high reliability at r value = (0.80) in the current study. This means that the tools are stable and reliable.

The pilot study was conducted for the period from 9th January 2022 to 16th January 2022. The pilot study was conducted prior to the start of the study and consisted of (20) infants who were selected purposively from Mosul primary health care Centers.

According to the results of this pilot study, a final fine adjustment of the questionnaire form was done. This sample was excluded from the study.

Statistical analysis

Statistical data analysis was done by Statistical Package for Social Sciences (SPSS) version 25. A descriptive approach was applied. Frequency and percentage were computed. The Chi-square test was computed to find the associations for certain categorical variables.

Ethical issues

Following preliminary approval from the College of Nursing at the University of Mosul, the study received final approval from the Ethical Research Committee housed within the Nineveh Health Directorate. Before any data collection took place, each participant provided their informed consent.

Results

Table 1: Demographical Characteristics of studied infants (n=140)

Variables		Case n=70		Control n=70	
		No.	%	No.	%
Age Group (months)	1-3	43	61.4	43	61.4
	< 3-6	11	15.7	11	15.7
	< 6-9	11	15.7	11	15.7
	< 9-12	5	7.1	5	7.1
	X^2 = 0.000	P. value = 1.000			
Gender	Male	50	71.4	50	71.4
	Female	20	28.6	20	28.6
	X^2 = 0.000	P. value = 1.000			
Gestational age	Premature	45	64.3	8	11.4
	Full-term	25	35.7	62	88.6
	X^2 = 41.566	P. value = 0.000			
Twin	Yes	8	11.4	0	0.00
	No	62	88.6	70	100.0
	X^2 = 8.485	P. value = 0.004			
Order of infant in the family	First	31	44.3	10	14.3
	Second	15	21.4	6	8.6
	Third	11	15.7	49	70.0
	More than	13	18.6	5	7.1
	X^2 = 42.235	P. value = 0.000			
Consanguinity between father and mother	Relative	52	74.3	13	18.6
	Not relative	18	25.7	57	81.4
	X^2 = 43.680	P. value = 0.000			

Note: No: Number, %: Percentage, X^2: Chi-Square, Sig.: P. value.

Table 1: showed that 61.4% of infants with reflux were within the 1-3 months age group, and 71.4% of studied infants with GER were male. Premature infants had a significant more frequency of having GER in comparison to full-term infants; twins significantly had GER more frequently than singleton infants, firstborn infants also had GER significantly more than comparable groups, and infants born from consanguineous marriages had GER significantly more than the non-consanguineous ones.

Table 2: Hypothesized risk factors for gastroesophageal reflux among studied infants (n=140)

Variable		Case n=70		Control n=70	
		F.	%	F.	%
Use of warping	Yes	61	87.1	14	20.0
	No	9	12.9	56	80.0
	X^2 = 63.438		P. value = 0.000		
Exposure to smoking	Yes	56	80.0	5	7.1
	No	14	20.0	65	92.9
	X^2 = 75.563		P. value = 0.000		
Family history of asthma	Yes	21	30.0	0	0.0
	No	49	70.0	70	100.0
	X^2 = 24.706		P. value = 0.000		
Starting setting position for infants	Not start setting	53	75.7	56	80.0
	Setting with support	6	8.6	0	0.0
	Setting without support	11	15.7	14	20.0
	X^2 = 6.443		P. value = 0.040		
Use of pacifier	Yes	14	20.0	44	62.9
	No	56	80.0	26	37.1
	X^2 = 26.493		P. value = 0.000		

Note: No: Number, %: Percentage, X^2: Chi-Square, Sig.: P. value.

Table 2: shows there significant statistical differences between case and control groups; regarding studied variables.

Discussion

Regarding infant's age and gender, there are no statistical differences between the case and the control sample as they were age-group matched and gender-matched. Table 1: illustrates that there were (64.3%) of premature infants in case group with statistically significant differences(p value= 0.00) in comparison to (11.4%) of premature infants in the control group; other investigators had the same conclusion [10]. The most common risk factor for GER is the physiologic consequences of prematurity, as these infants have an increased risk of GER events secondary to increased respiratory effort and transient increase in intra-abdominal pressure resulting from airflow obstruction, this causes the LES tone to decrease and in turn contributes reflux [11].

Table 1; illustrated that (11.4%) of twin infants with GER were statistically significant differences (p value=0.004) in comparison to (0.0 %) of not twin infants in the control group other investigator had the same conclusion [12]. In addition to that, it is worthy to illustrate that, each of the four twins in this study was of identical gender which suggests the presence of monozygotic twinning; and implies the existence of a 100% concordance rate among twins

Table 1 displayed that (44.3%) of GER infants were the first infant were statistically significant difference (p-value = 0.000) in comparison to (7.1%) of more than third order of the healthy infants, this finding might be due to increased experience of a mother in dealing with their regurgitated infant, bearing in mind that there was 91.4 % frequency of positive family history of GER.

Table 1 demonstrated that (74.3%) of the consanguineous parents of infants having GER were statically significant difference (p value=0.000) in comparison to (25.7%) of those who were not consanguineous parents of healthy infants; which agreed with other investigators [13] that found family studies have revealed an about 31% heritability of the disease. Numerous single-nucleotide polymorphisms in various genes like FOXF1, MHC, CCND1, anti-inflammatory cytokine and DNA repair genes have been strongly associated with increased GER risk [14].

Table 2 showed that (87.1%) of mothers of GER infants wrapped their infants with a statistically significant difference (p-value = 0.000) in comparison to (80%) of mothers of healthy infants were didn't wrap their infants. Table 2 clarified that (80%) of infants having GER were exposed to smoking with a statistically significant difference (p value=0.000) in comparison to (92.9%) of the healthy infants who were not exposed to smoking. Other investigators reached to a same conclusion [15] [16]. GER has a greater occurrence in infants exposed to smoking because tobacco smoking can reduce the lower esophageal sphincter pressure, facilitating reflux. In addition, tobacco smoking reduces the production of saliva rich in bicarbonate, which is important for buffering and clearance of acid in the esophagus [17].

Table 2 revealed that (30%) of GER infants had a family history of asthma with a statistically significant difference (p-value = 0.000) in comparison to healthy infants having no family history of asthma. To the best of our knowledge, there is no previous study linking the family history of asthma to the occurrence of GER in subsequent generations. Although it is well known that GER is one of the comorbidities that trigger asthma in the index case.

Table 2 elucidated that (8.6%) of infants having GER started setting position (with support) had a statistically significant difference (p value=0.040) in comparison to (0.0%) of the healthy infants were not start setting position (with support). Start setting position early increases the occurrence of GER Because In small infants with poorly developed truncal control, sitting upright can lead to slumping, which in turn may increase intra-abdominal pressure and reflux [18].

Table 2 showed that (80 %) of GER infants were not using pacifier and with a statistically significant difference (p value =0.000) in comparison to (62.9%) of

healthy infants who were using pacifier, indicating that pacifier had a protective role against devolvement of infantile GER with a relative risk of 6.8(O.R:6.769 ;95 CI: 3.165-14.479) implying that pacifier users infant is about seven times protected from GER in comparison to non-pacifier users. other investigators [19] advised that pacifier may be reasonably used in preterm neonates with symptoms of gastro-esophageal reflux.

Conclusion

Throughout the course of the current study, a number of potential risk variables have been identified. These risk factors include having a twin, using wrapping, being exposed to smoking, having a family history of asthma, using pacifiers, and starting setting position for newborns. Recommendations include keeping infants away from smoking environments and avoiding the use of restrictive wrapping.

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