Original Article

Investigation of a collective food poisoning in the province of Kenitra - Morocco from 2019 to 2023: A study to determine the epidemiological profile and the effectiveness of the management measures implemented

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ABSTRACT

Aim

The objective of this study is to examine collective foodborne illnesses (TIAC) reported in province of Kenitra from 2019 to 2023, with the aim of determining the epidemiological profile and evaluating the effectiveness of the management measures implemented. On August 5, 2019, the survey therefore highlighted 9 cases (response rate of 75%), with an average age of 29 years and 75.5% women. Nausea, abdominal pain, diarrhea and vomiting were the main symptoms. The study revealed a significant correlation between the consumption of fish (75% attack rate), fries (90%) and soda (80%). Likewise, the study conducted on February 1, 2022 revealed a significant correlation between intoxication and consumption of soup (RR=1.4), chicken (RR=2.4), salad (RR= 1.62) and bread (RR=2.4).

Rice presents a higher risk (RR=5.1, p=0.05). Levels of staphylococcus aureus were detected during microbiological analyses, exceeding acceptable thresholds. Faced with these findings, monitoring of food safety practices seems necessary. Preventing these outbreaks in the future would be most effective by improving food handling, storage and preparation methods.

Keyword

collective food poisoning; epidemics; Kenitra; Morocco.

INTRODUCTION

Food poisoning results from the consumption of foodstuffs contaminated by pathogenic germs, common germs and/or their toxins ¹. More precisely, collective foodborne illnesses (TIAC) are acute poisonings which occur after the ingestion of food contaminated by bacteria or their toxins, viruses, parasites or certain heavy

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metals. They are defined by the appearance of at least two manifestations, generally digestive symptoms, attributable to the same food source². TIACs are notifiable communicable diseases ¹.

TIAC represents a major public health problem on a global scale, and this problem is particularly pressing in our country³, especially during the summer season. The appearance of a TIAC causes great concern, particularly when it creates a large outbreak and leads to numerous hospitalizations. For example, in the United States, approximately 5760 outbreaks were reported between 2009 and 2015, resulting in 100,939 cases, 5699 hospitalizations, and 145 deaths4. In Brazil, almost 13,163 cases were reported from 2000 to 2008, involving 247,570 cases and 195 deaths ⁴. In the Netherlands, approximately 5657 outbreaks were reported from 2006 to 2019, including 27,711 cases ⁵. Similarly, in China, 1001 outbreaks of foodborne illnesses were reported in 2013, resulting in 14,413 illnesses and 90 deaths ⁶. In 2021, the number of outbreaks increased to 5493, with 32.334 cases and 117 deaths ⁷.

MATERIAL AND METHODS

Between 2019 and 2023, the province of Kenitra experienced three separate incidents of collective foodborne illness. Each of these incidents occurred on different dates and in different settings:

- 1. The first incident occurred on Monday August 5, 2019. Nine employees of a factory were admitted to the emergency room of IDRISSI Hospital in Kenitra. They experienced symptoms such as abdominal pain, vomiting and diarrhea. All affected employees had eaten their meals in the factory canteen.
- 2. The second incident took place on Tuesday February 1, 2022. This time, six students from the Preparatory Class of Lycée Med VI Kenitra were admitted to the emergency room of IDRISSI Hospital. They had similar symptoms to the previous incident. The affected students had taken their meals in the high school canteen.
- 3. The third incident occurred on February 15, 2023. Three other students from the Preparatory Class of Lycée Med VI Kenitra were admitted to the emergency room of Idrissi Hospital with symptoms similar to the two previous incidents. These students had also eaten their meals in the canteen.

For each of these three incidents, an investigation was

carried out to identify the origin of the contamination. Samples and analyzes of the meals served were taken. The information collected includes the identification of affected people (age, gender), times of onset of symptoms, their evolution, foods consumed, etc.

Data analysis

Data entry and statistical analysis of the questionnaires were carried out using SPSS software for descriptive analysis. First, the cohort of people who participated in the meals was described in terms of age, sex, clinical symptoms and severity. In order to describe the epidemic episode, attack rates (AT) were calculated overall then by meal and by food.

From the case definition, the epidemic curve was constructed and the clinical signs declared by the cases were described in order to formulate hypotheses on the pathogens potentially causing the declared symptoms. Secondly, a univariate analysis was carried out. Its objective was to highlight the existence or not of a statistically significant association between the occurrence of clinical signs and the consumption of one or more of the foods served in the factory canteen.

The association measures (relative risk (RR)) were calculated, accompanied by their confidence intervals at the 5% threshold. The degree of significance (p-value) was also calculated using the Chi2 test. The significance level was set at 5%.

Microbiological analyzes of foods

The analyzes included the search for pathogenic germs likely to be the cause of TIAC: sulfito -reducing Clostridium, staphylococcus aureus, salmonella and Listeria monocytogenes as well as the search and quantification of Escherichia Coli, an indicator of the general conditions of hygiene when preparing food.

The canteen kitchen was inspected by the CPE and the Provincial Environmental Hygiene Unit to identify conditions likely to have contributed to the TIAC.

Results of the 1st poisoning:

Results of the epidemiological investigation

Among the 12 employees in the group from 7 a.m. to 7 p.m., 9 responded to the questionnaire, representing a response rate of 75%. The average age of the participants was 29 years [20-48 years]. 75.5% of participants were women.



In total , 9 people out of the 12 participants reported having been ill (according to the case definition) in the hours following lunch on Monday August 5, 2019 and only 8 women and 1 man consulted the emergency room without being hospitalized. The overall attack rate was 57.62%.

Clinical symptoms

Table 1 details the frequency of symptoms among patients. Among the 9 cases, the clinical symptoms were mainly nausea (88.889 %), abdominal pain (77.778 %), diarrhea (100%) and vomiting (66.667 %).

Table 1: Frequency of occurrence of symptoms in all cases (n=9)

Variable\Statistic	Workforce by modality	Frequency by modality (%)				
Symptom	9	100				
Nausea	8	88,889				
vomiting	6	66,667				
abdominal pain	7	77,778				
Diarrhea	9	100				
Headache	8	88,889				
Dizziness	8	88,889				
Burning	9	100				
Itchy	8	88,889				
Eruptioncu	6	66,667				

Epidemic curve

The epidemic curve at a time interval of half an hour was established on the basis of the declaration by patients of the time of the appearance of the first clinical signs (Figure: 1).

5 4 -985 3 1 1 14:00 14:30 15:00 15:30 16:00 16:30 17:00 17:30 18:00 18:30 19:00 Start time of symptoms

Figure 1: Epidemic curve of collective food poisoning in a factory, Lalla mimouna, O5 August 2019

It indicates that the first cases presented digestive signs on August 5 at 3:00 p.m. The peak in the occurrence of cases was around 2:30 p.m. followed by a decrease in the number of cases until 6:30 p.m. Shown in red are the time markers indicating the consumption of meals suspected of being the cause of TIAC (2:00 p.m).

From the epidemic curve we can deduce that it is a common point source. The incubation time varies between 1 hour and 3.5 hours. At this stage of the analysis. if the lunch of August 5 was in question and taking into account the symptoms that appeared and the incubation period, the hypothesis of contamination by Staphylococcus aureus from one or more foods was to be verified.

Univariate analysis

Univariate analysis carried out revealed a statistically significant association between the occurrence of the disease and the consumption of lunch on 08 as shown in Table 2.

Table 2: Association between meal exposure and disease

W 1	Have consumed		Did not consume			RR	95% CI	P		
Meal	Total	Case	Attack Rate %	Total	Case	Attack Rate %	KK	95% CI	r	
Breakfast from 04-08	12	8	66.67	1	1	100	5.5	[1.37-6.30]	0.32	
Lunch from 04-08	3	1	33.33	6	1	16	1.67	[0.19-2.13]	0.76	
Breakfast from 05-08	11	9	81	1	0	0	5.58	[1.22-4.76]	0.27	
Lunch from 05-08	11	9	81	1	0	0	6.02	[1.22-11.3]	0.005	



Table 2 presents, for the entire population of respondents, the attack rates among consumers and non-consumers of meals on August 4 and 5 (breakfast and lunch) taken in the factory canteen, in addition to the relative risks associated with the consumption of these meals, their confidence intervals and their p-value.

This analysis made it possible to incriminate the lunch

of August 5 with an attack rate of 81% among the employees who consumed it. Among those who did not consume it, the attack rate was 0%. The relative risk associated with the consumption of this meal was 6.02 (95 % CI [1.22-34.68]; p<0.05). Following this observation, the same analysis is carried out for each food constituting the lunch of August 5.

Table 3: Numbers and proportions of food consumption among cohort participants; association indicators (RR), confidence interval and p-value

	Have consumed				Did not c	onsume	RR	95% CI	P
	Total	Case	Attack Rate %	Total	Case	Attack Rate %	KK	95% CI	1
Fries	10	9	90	2	0	0	3.2	[1.73-5.84]	< 0.001
Pisces	12	9	75	3	1	33.33	4.3	[1.68-8.02]	< 0.001
Hot sauce	10	5	50	2	1	50	1.4	[1.27-1.30]	0.02
Ketchup	6	1	16.67	6	2	66.67	1.54	[3.03-6.93]	0.32
Mayonnaise	8	1	12.5	2	0	0	1.43	[4.02-6.43]	0.12
Soda	10	4	40	2	1	50	2.65	[4.45-5.43]	< 0.001
Bread	8	1	12.5	4	3	75	1.7	[1.32-2.04]	0.03
Mustard	11	7	63.64	1	0	0	1.94	[1.55-4.83]	0.23
Salad	12	7	58.33	0	0	UND	UND	UND	< 0.01

Attack rates were high and varied depending on the type of food consumed. We noticed an attack rate of 75% for fish and 90% for fries among those who ate them. At this stage of the analysis, a statistically significant association was found with the consumption of 3 foods from the August 5 lunch. These were fish (RR=4.3), fries (RR=3.2) and soda (RR=1.8).

In total, these analyzes highlighted several foods potentially involved in the occurrence of TIAC. The strongest associations were observed for fish (attack rate 75%) and fries (attack rate 90%) with low attack rates among people who did not consume these foods: 33.33 % for fish and 0% for fries.

Results of 2th poisoning

Results of the epidemiological investigation

Among the 100 students, 40 responded to the questionnaire, representing a response rate of 40%. the age of the participants was 18 years old. 56% of participants were girls.

In total, 6 people out of the 40 participants reported having been ill (according to the case definition) in the hours following lunch on Monday February 1, 2022 and only 1 woman and 5 men consulted the emergency room without being hospitalized. The overall attack rate was 15%

Clinical symptoms

The table indicates that all 6 cases studied had symptoms such as vomiting and abdominal pain. However, the frequency of diarrhea is 66%, which means that 4 of 6 cases also have this specific symptom.



This suggests that diarrhea is not present in all patients, but is seen in a majority. Importantly, the remaining two cases did not present with diarrhea, which may indicate variation in the manifestation of symptoms among the patients studied.

Table 4: frequency of occurrence of symptoms in all cases (n=6)

Variable\Statistic	Workforce by modality	Frequency by modality (%)			
Symptoms	6	100			
Vomiting	6	100			
Abdominal pain	6	100			
Diarrhea	4	66%			

Epidemic curve

Patient declarations on the appearance of the first clinical signs were used to establish the epidemic curve (Figure 2). We can observe in this curve that the first cases were accompanied by digestive symptoms. A peak of cases is reached around 4 p.m., then the number of cases decreases after an increase between 5:30 p.m. and 7 p.m. Time markers indicating suspicious meals, which took place at 1:30 p.m., are marked in red. By observing this epidemic curve, it is possible to conclude that it is an occasional common source. Incubation can last 2.5 to 4 hours.

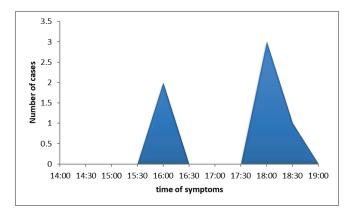


Figure 2: Epidemic curve of collective food poisoning of students, Lycée Mohamed IV

At this stage of the analysis, if lunch is probably responsible for the symptoms observed and taking into account the incubation period, it is necessary to verify the hypothesis of contamination by Staphylococcus aureus from one or more foods.

Univariate analysis

The association between meal exposure and disease is highlighted in Table 2, particularly breakfast and lunch on February 1. The table displays the following data: This suggests that there is a potentially important link between consumption of this meal and the onset of illness.

Similarly, the relative risk for lunch on February 1 is 5.03, with a confidence interval of [1.64-6.2] and a p-value of 0.005, suggesting a statistically significant correlation between both.

On the other hand, the links between meals on January 31 and disease do not present statistical significance, as evidenced by the relative risk, confidence interval and p-value values. These results indicate that there is a link between eating breakfast and lunch on February 1 in the high school canteen and a higher risk of illness, while eating meals on January 31 does not appear to have a link, evident with illness.

Food consumption among cohort participants during collective poisoning is given in Table 3, as well as measures of association (relative risk – RR), confidence intervals (95% CI) and values from p. - The relative risk of soup consumption is 1.4 (95% CI: [1.32-1.43], p < 0.001). - Chicken is linked to a relative risk of 2.4 (95% CI: [1.24-1.42], p < 0.001), which suggests a higher risk of collective poisoning among individuals who have consumed chicken compared to those who did not consume it.

- Regarding rice, despite a relative risk of 5.1 (95% CI: [1.22-1.43]), the p-value is 0.05, which suggests that there is a possible, but not statistically significant, correlation between rice consumption and collective intoxication. - Consumption of salad is associated with a relative risk of 1.62 (95% CI: [1.42-1.34], p < 0.001), indicating an increased risk of collective poisoning among people who consumed salad. salad compared to those who did not consume it. Finally, we observed a relative risk of 2.4 (95% CI: [1.32-2.04], p < 0.001), which suggests a higher risk of collective poisoning among individuals who consumed bread compared to those who did not consume it.

In summary, Table 3 highlights significant correlations between consumption of soup, chicken, salad and bread and collective drunkenness. Rice consumption is potentially related, but it is not statistically significant. According to these results, it is possible that these foods are responsible for the collective poisoning studied.



Table 5: Association between meal exposure and disease

Meal	Have consumed			Did not consume					
	Total	Case	Attack Rate %	Total	Case	Attack Rate %	RR	95% CI	P
Breakfast from 31-01	12	1	8.33	4	0	0	1.3	[1.02-6.30]	0.15
Lunch from 31-01	5	1	20	9	1	11	1.26	[1.32-6.31]	0.84
Breakfast from 01-02	14	4	28	3	0	0	3,545	[1.43-4.30]	0.11
Lunch from 01-02	10	6	60	5	0	0	5.03	[1.64-6.2]	0.005

Table 6: Numbers and proportions of food consumption among cohort participants; association indicators (RR), confidence interval and p-value

	Have consumed		1	Oid not co	nsume	RR	95% CI	P	
	Total	Case	Attack Rate%	Total Case Attack Rate %		KK			
Soup	10	5	90	1	0	0	1.4	[1.32-1.43]	< 0.001
Chicken	8	6	75	5	0	33.33	2.4	[1.24-1.42]	< 0.001
Rice	10	2	50	3	1	50	5.1	[1.22-1.43]	0.05
salad	7	4	16.67	5	0	66.67	1.62	[1.42-1.34]	< 0.001
Bread	10	6	12.5	2	0	75	2.4	[1.32-2.04]	< 0.001

Results of the 3rd intoxication

The study on collective intoxication revealed three cases of intoxication, which occurred as part of an incident at high school. However, it is interesting to note that despite these incidents, none of the participants interviewed reported experiencing symptoms.

Theage of the students involved in this study is 18 years old. Additionally, it was mentioned that the foods eaten in the high school canteen were chicken, minced meat and rice. The symptoms of the three cases of poisoning identified are identical, which suggests consistency in the responses of the participants concerned.

Results of the veterinary investigation

The microbiological analyzes of the food were carried out as part of the veterinary investigation, The stool cultures were not carried out on the patients nor the vomit samples or other biological analyses, The food taken on August 5, 2019 in the kitchen of the canteen were the subject of a microbiological analysis. However, during the visit to the scene of the two poisonings, which occurred respectively on February 1, 2022 and February 15, 2023, the samples necessary for the analyzes were not available. They were carried out with the aim of detecting pathogenic microorganisms such as such as Escherichia coli, sulfito -reducing Clostridium, staphylococcus aureus, salmonella and Listeria monocytogenes.

Of all the analyzes carried out, the presence of staphylococcus aureus was detected in 2 foods consumed during lunch on August 5: fish 5 10 ² g ⁻¹) and fries (4.5 102g ⁻¹) in levels exceeding the threshold of acceptability according to national and international standards and Moroccan microbiological criteria (joint



Table 7: frequency of occurrence of symptoms in all cases (n=3)

Variable\Statistic	Distribution by subsample (%)	No. terms	Fashion	Mode (effective)	Terms	Workforce by modality	Frequency by modality (%)
Symptom	100	1	Yes	3	Yes	3	100
Vomiting	100	1	Yes	3	Yes	3	100
Abdominal pain	100	1	Yes	3	Yes	3	100
Diarrhea	100	1	Yes	3	Yes	3	100

decree No. 624-04 of 17 Safar 1425 and April 8, 2004).

Other foods which were part of the canteen menu, and which were consumed during breakfast on August 5, also had high levels of staphylococcus aureus, this is the case of the salad whose germ content exceeded the threshold of acceptability (1.2 106 g⁻¹).

E. Coli was found in 6 foods among the 10 analyzed, namely fries and fish, but in quantities not exceeding the acceptable threshold. For other foods (rice salad, beetroot salad, poop salad), the detected level of E. Coli exceeded the acceptability threshold. The presence of E. Coli is an indicator of fecal contamination and poor general hygiene conditions

The analyzes carried out from these samples did not reveal the presence of sulfito -reducing Clostridium, salmonella or Listeria monocytogenes.

Possible contamination of fish and fries at the time of preparation by the cooks could not be verified given the impossibility of taking samples for all the staff or even consulting the medical files of the kitchen staff. the canteen in order to detect the presence of healthy carriers. However. The lack of hygiene in the kitchen premises was noted during their inspection. In addition, the contamination of food by E colt is in favor of non-compliance with hygiene rules and therefore the contamination of food during the preparation process. Following the completion of the veterinary investigation, a letter was sent to Kenitra to the factory managers to inform them of the report of the investigation.

DISCUSSION

Collective foodborne illnesses are a major public health problem worldwide [8,9] . An outbreak of TIAC is defined by the appearance of at least two grouped cases, with similar symptoms, generally digestive, the cause of which can be attributed to the same food origin (except for botulism where one case is enough to trigger alert) 10,11 .

We conducted a study on collective food poisoning from 2019 to 2023. In 2019, we observed 9 cases, 6 cases in 2022 and 3 cases in 2023. The years 2020 and 2021 were marked by the coronavirus pandemic, which had a significant impact on recorded cases of collective food poisoning. With social distancing and travel limitations imposed to limit the spread of the virus, many people have had to prepare and consume meals at home 12.

This situation had several consequences. First, it is likely that cases of collective food poisoning were not reported or detected as systematically during this period. Temporary closures of restaurants, cafes and other food service establishments have led to a reduction in outdoor dining, where the risks of food poisoning may be higher.

Additionally, hygiene and food safety measures implemented in households, such as frequent hand washing, proper food handling and proper cooking, have helped reduce cases of poisoning 13.

Additionally, it is worth noting that symptoms of coronavirus disease, such as fever, stomach upset, nausea and vomiting, can be similar to those of food poisoning. This can lead to confusion in diagnosing and reporting cases, particularly when coronavirus tests are not widely available or used 14.

Our investigation into the 1st poisoning on August 5, 2019 showed that it is indeed a TIAC which affected a large number of people with an overall attack rate of 75%. Higher rates have been calculated for specific foods such as fish with an attack rate of 75%. This is a high



rate characterizing TIAC caused by staphylococci with attack rates of up to 85% ¹⁵.

During the first collective food poisoning, the main clinical signs observed were abdominal pain, nausea, diarrhea and vomiting which resolved quickly. Only nine people visited the emergency department without requiring hospitalization, indicating a low-severity outbreak. The epidemic curve suggests a point source, that is to say that there was a specific source of contamination. The short incubation period, which was 1 to 3.5 hours, is indicative of possible infection with enterotoxin-producing bacteria, such as Staphylococcus aureus ⁹, ¹⁰.

For the second food poisoning that occurred on February 1, 2022, the affected students were on average 18 years old. The percentage of people affected was 15%. Among the six cases identified, diarrhea was present in four of them, which corresponds to a frequency of 66% for this specific symptom. Incubation of the disease could vary from 2.5 to 4 hours, meaning that symptoms began to manifest in affected individuals within this time window after their exposure to the pathogen or contaminant 10, 16 . Staphylococcal foodborne illness is one of the most common foodborne illnesses 17,18 . It is a major concern in public health programs worldwide 17. A typical TIAC caused by S.aureus has a rapid onset after ingestion of contaminated food (usually 1-3.5 hours). 1. This is due to the ingestion of preformed enterotoxins in the food which are generated by bacteria during growth at favorable temperatures 10 These enterotoxins are resistant to digestive juices and heat while the bacteria is heat sensitive Foods can be contaminated by the hands of healthy or infected carriers who handle them or by contact with contaminated raw material, equipment or surfaces. Finally, the definitive diagnosis of Staphylococcus aureus TIAC is based on the detection of staphylococcal enterotoxins in food 19, or the recovery of at least 103 S.aureus g-1 from food remains. This study is consistent with Koudio 's study Kouassi in Ivory Coast 20.

In our investigation, we did not perform toxicological analyzes to confirm the presence of enterostomy. However, the microbiological results obtained were in agreement with the epidemiological data, suggesting a contamination scenario during food preparation. In particular, a significant correlation was observed between the presence of staphylococcus aureus

exceeding acceptability thresholds and certain foods such as fish and chips.

Foods that require intense handling during preparation, such as fish in this case of food poisoning, have been shown to be frequently associated with staph poisoning. Food handlers are often the main source of contamination in cases of staph poisoning.

Main strengths and limitations of this study Main strengths

During this TIAC, the alert was launched early and the first measures and recommendations were issued quickly by the CPE which made it possible to prevent the occurrence of new cases. The response rate estimated in the retrospective cohort study was good since almost ½ of the people who consumed the meals answered the questionnaire face to face[21];

-Active case research was carried out in partnership with plant managers. The questioning of the cases made it possible to limit the response biases linked to the completion of a self-questionnaire. In addition, the time between the consumption of the dishes and the questioning of the cases was short (4 to 8 days), which limits memorization bias.

Main limitations of the study

-The fact that the symptoms were not very serious and resolved quickly did not favor biological samples from the patients. Indeed, carrying out microbiological examinations in the patients can make it possible to compare the strain found in them to that found in the food, in order to be able to provide arguments in favor of a causal link if the dietary and biological results agree.

-The limited collaboration of the company's administration did not make it possible to investigate various avenues, or to test or validate the hypotheses put forward from the cross-referencing of epidemiological, veterinary and microbiological data.

-In addition to these limits, certain biases linked to the retrospective nature of the investigation, in particular the biases of prevarication or convenience conditioned by the relations between the employees, the factory administration and the company in charge of factory level restoration.



VII. Conclusions and recommendations

This investigation confirmed the occurrence of a TIAC on August 5, 9 cases recorded as part of the lunch served the same day in the canteen of a factory in Kenitra ²². This TIAC illustrates the very strong impact of noncompliance with hygiene practices by a subcontracting company responsible for the preparation of collective meals in the workplace. Two foods served in the canteen at the origin of the contamination were able to be identified, these are fish and fries, the consumption of which is significantly associated with the fact of having developed a sudden and rapid digestive syndrome on the day of the meal. This clinical picture suggested a toxin syndrome linked to the significant presence of Staphylococcus aureus in these foods.

The main recommendations that can be made following this TIAC are:

- -Apply hygiene measures when preparing meals and handling food, systematic and regular washing of hands when preparing meals, wearing gloves.
- -Identify and remove sick catering staff and ensure their good health before resuming their activity in the kitchen;
- -Communicate quickly with the people concerned to inform them of the situation and the measures taken.
- -Combine epidemiological, veterinary and microbiological investigations and launch as soon as possible, after the outbreak is declared, requests for biological examinations in patients (stool cultures)

in order to be able to validate hypotheses and guide management actions on the ground.

Overall, this investigation highlights the interest in early association of the epidemiological, veterinary and microbiological aspects and the first management measures, in order to avoid major consequences in collective catering.

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CONFLICT OF INTEREST

The authors assert that there are no conflicts of interest associated with this research.

ETHICAL CLEARENCE

There was no need for ethical clearance for this research.

AUTHORSHIP CONTRIBUTION

Asmaa Elkhal: Acquisition of data, data analysis, interpretation of results, writing-original draft and submitting manuscript, Badreddine Dahou: involved in writing, reviewing, Abdelkader Chibani: reviewing, Nabila Auajjar, Benaissa Attarassi.: supervision and writing-review, Sanae Sadek: supervision and writing-review, Nabila Auajjar, Benaissa Attarassi: interpretation of results, writing-original draft, reviewing and editing. All authors have read and agreed on the final version of the manuscript



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