Does fasting during Ramadan increase the risk of developing Sialadenitis?

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Abstract

Background: Ramadan is the ninth month within the Islamic lunar calendar, where Muslims are required to fast (abstain from food and drink) during the daytime (from sunrise to sunset) for the entire month. Due to connection between fasting, dehydration and siaadenitis, the aim of this study is to determine if there is a higher frequency of siaadenitis among the Muslim population during Ramadan compared to other months of the year.

Methods: We conducted a retrospective cross-sectional study using the medical records of 120 Muslim patients admitted through the emergency room (ER) with a diagnosis of siaadenitis over a 5-year period at the Baruch Padeh Medical Center, Poriya and St. Vincent de Paul Hospital, Nazareth – both located in Israel.

Results: During the month of Ramadan the admission of Muslims through the emergency room (ER) with a diagnosis of siaadenitis was more than doubled compared to other months of the year – a difference that was found to be statistically significant (p=0.001). Additionally we found that Ramadan patients had significantly higher Leukocyte numbers at admission (p=0.0085) and importantly a significantly higher level of dehydration (BUN/Creatinine rate) (p=0.0001).

Conclusion: There is evidence that fasting in Ramadan may increase the risk for developing siaadenitis compared to non-fasting months. Our results suggest that this may be the result of dehydration.

Background

Ramadan is the ninth month within the Islamic lunar calendar, where Muslims are required to fast (abstain from food and drink) during the daytime (from sunrise to sunset) for the entire month.[1] Ramadan fasting represents a particular form of fasting, in that it consists of alternate fasting and feasting (re-feeding) periods.[2] Being based on the lunar calendar, the daily fasting duration varies depending on the period of the year and the latitude of the location.[3] There are several previous reports about metabolic changes associated with fasting, like weight loss and dehydration.[4, 5] Those changes may primarily affect Diabetes patients [6], but also there are reports that Ramadan fasting may cause hyprtension [7] and increase ischemic stroke incidence.[8]
However, for healthy individuals, these changes are not likely to have significant harmful consequences on healthy individuals.[9, 10] Even though infirm individuals are waived to take part in this religious duty, patients with various health problems, might choose to share this event with peers and family members.[11]

Acute sialadenitis is a bacterial inflammation of the salivary gland. Stasis of salivary flow secondary to dehydration or decreased oral intake allows bacterial migration into the gland parenchyma.[12] Dehydration can be assessed through blood hydration status markers, especially Blood Urea Nitrogen(BUN)/Creatinine ratio.[13, 14]

Given the connection between dehydration and sialadenitis, we hypothesized that there is a higher frequency of sialadenitis among the Muslim population during Ramadan compared to other months of the year. This study, to the best of our knowledge, is the first study investigating the connection between Ramadan and incidences of sialadenitis. The hospitals involved in this study are uniquely positioned to address the hypothesis that Ramadan fasting corresponds to an increased frequency of sialadenitis since a large portion of their patient base are Muslim. Poriya MC is an Israeli Ministry of Health-owned public hospital serving the area of Eastern Galilee and Golan Heights and a multi-regional center for Oral and Maxillofacial Surgery. It is estimated that 40–60% of its patients come from the Muslim community. Nazareth French Hospital is a Catholic Church Trust-owned public hospital located in the heart of Nazareth, the largest Arab city in Israel, and has an exclusive otolaryngology service in that area. More than 80% of its patients come from the Muslim community.

Methods
This study was approved by Poriya Medical Center Institutional Review Board (approval # POR-18-0061). The research sample included all adult (>14 yrs) cases of sialadenitis (identified by the International Classification of Diseases, Ninth Revision (ICD-9) code 527.2—Sialadenitis) diagnosed in Muslims (data on patient religion was received from the Israeli Ministry of Interior database) in the Emergency Rooms of Baruch Padeh Medical Center, Poriya and St. Vincent de Paul (French) Hospital, Nazareth (both affiliated to the Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel and located in Northern part of Israel) during the Hijri years 1434-1438 (15/11/2012–20/09/2017). The age
filter was chosen to increase the probability of fasting and to rule out juvenile conditions.

For this sample (sialadenitis diagnosis, Muslim, < 14 years age) we calculated the frequency of ER admissions for each Hijri month in the timeframe and compared Ramadan months to other months of the year. For the sake of accuracy, analysis was carried out based on Hijri calendar months since the month of Ramadan is part of this lunar calendar which is 11 days shorter than standard Gregorian solar calendar. It is important to note that we cannot be sure of the fasting status of each patient, but given that Ramadan fasting is the normal social custom practiced by the vast majority of Israeli Muslims we assume that the majority of the patients included in this study were fasting during the month of Ramadan.

Additionally, in order to exclude the possibility of co-morbidities whose prevalence may rise in an older population, we assessed for significant differences in the mean age of patients admitted during Ramadan and during other months of the year.

Statistics were calculated using MS Excel (2010 version) and SPSS (25.0 version) software for MS Windows. The comparison between subgroups was made using non-parametrical tests: ANOVA, t-test, Kruskal-Wallis test, Wilcoxon Signed Ranks test, Fisher’s Exact test, Mann-Whitney U test. Adjustment factors were calculated by Pearson method. A probability of <0.05 was considered significant.

Results

Our data showed that 21 Muslims were admitted to the ER in aforementioned hospitals during the 5 Ramadan months in the timeframe of the study, revealing an incidence of 4.2/month (95% CI 2.641–6.176). This was high compared to non-Ramadan admissions; 99 admissions in 55 non-Ramadan months resulting in an incidence of 1.8/month (95% CI 1.471–2.166). The risk ratio (RR) of ER admission due to sialadenitis during Ramadan was 2.33 (95% CI 1.46–3.72) and statistically significant (p = 0.001). The prevalence curve among months is presented in Figure 1.

The variables and statistic analysis is detailed in Table 1. Comparing blood test results of Ramadan vs. Non-Ramadan Patients revealed that Ramadan patients have significantly higher mean Leucocytes numbers [*10^9/L] (8.98±2.75 vs. 6.08±4.78, p = 0.0085) and significantly higher mean Creatinine[mg/dL] (0.81±0.33 vs. 0.62±0.13, p = 0.0001) and mean BUN[mg/dL] (14.26±3.85 vs.
5±2.08, p = 0.0001) levels. The combined mean BUN/Creatinine ratio was significantly higher in Ramadan patients (17.7 vs. 8.06, p = 0.0001). There was no difference in Amylase rates [U/L] (360±405.25 vs. 370.25±398.81, p = 0.915).

The mean age of Ramadan patients was 42.88 ± 16.7 years (SD, range 17–71), comparable to non-Ramadan patients whose mean age was 42.89 ± 22.02 years (SD, range 14–88). Also, there was no significant difference in M:F ratio or gland type prevalence among the two groups (Table 1).

Discussion
The results of this study show that the frequency of ER admissions due to sialadenitis significantly increases during Ramadan compared to non-Ramadan months over a multi-year analysis. Although, the authors were not able to find any previous report connecting Ramadan and salivary gland disorders, these results correspond with the known connection between sialadenitis and dehydration. Usually, acute sialadenitis affects one major salivary gland, the most prevalent being the parotid,[15] and is common in medically compromised, hospitalized, or postoperative patients. However, in this study the prevalence of Parotitis in lower than Sub-Mandibular Sialadenitis during Ramadan. It is however difficult to draw conclusions from this observed trend since the study group is small and the differences here were not statistically significant.

Another inciting etiology of sialadenitis is retrograde bacterial contamination from the oral cavity.[16] Predisposing factors for the ductally ascending infection are dehydration, xerogenic drugs and salivary gland diseases associated with ductal obstructions or reduced saliva secretion.[12, 17] Other factors include hypothyroidism, renal failure, diabetes mellitus and Sjögren syndrome. Salivary flow may also be reduced due to use of certain medications, especially those with anticholinergic properties.

Patients suffering from acute sialadenitis present rapid onset of pain and swelling of the affected gland. Physical examination may reveal edema, induration and extreme localized tenderness. Pressure on the gland may express pus from the respective intraoral orifice, requiring antibiotic therapy directed by pus culture.

Management of the condition involves treating the infection and reversing the underlying medical
condition and predisposing factors.[12] Salivary flow stimulation by hydration is highly important, as well as application of warm compresses, salivary gland massage, administration of sialagogues such as lemon drops or vitamin C lozenges and oral hygiene.[18, 19] The recommended initial empiric antimicrobial therapy is directed at gram-positive and anaerobic organisms by augmented penicillin that contains beta-lactamase inhibitors (e.g., amoxicillin-clavulanate [Augmentin]) helping treating penicillin-resistant bacteria. Possibly, culture-directed therapy is administered. Rarely, acute suppurative sialadenitis can lead to abscess formation; in those cases, surgical drainage is indicated.

The significant difference in BUN/Creatinine ratio and the fact that Ramadan patients presented dehydration hints that there is a connection between fasting and increased risk for sialadenitis. Analysis of Leukocyte count uncovered an interesting phenomenon; both groups presented normal Leukocyte counts, although that of the Ramadan group was slightly higher, that were “left shifted”, suggesting a bacterial infection. The Ramadan group seems to have the more serious condition, created by dehydration. This finding is also supported by systematic review showing that patients suffering from any condition that heighten the risk of developing infectious complications should not fast.[20]

These results of this study support our hypothesis and, assuming all other predisposing factors stay the same year-round, we conclude that there may be causality between Ramadan fasting (and subsequent dehydration) and increase in incidence of sialadenitis. We appreciate that physicians should also take into account the patient’s eagerness, since religion fosters positive psychosocial outcomes and reinforces treatment adherence and compliance in Muslim patients.[1, 20]

Thus, in the case of no medical restriction, fasting should not be discouraged in Muslim patients who are enthusiastic about Ramadan fasting. Physicians should be aware of this risk and patients should be instructed to recognize some warning symptoms.

This study has few limitations: First of all, it is a retrospective study, thus it was assumed that all of the patients were fasting during the month of Ramadan, but this was not confirmed. It will be useful to conduct a prospective study with documented fasting status (if ethically possible). Secondly, it is a
cross-sectional study, and thus it is difficult to establish causality, but rather only to look for any association between Ramadan and sialadenitis incidence. Finally, it will be useful to investigate a larger sample over a longer period in order to strengthen the findings in this study.

**Conclusions**

Our study indicates that fasting (and subsequent dehydration) in Ramadan may increase the risk for developing sialadenitis compared to non-fasting months. The Muslim population and their physicians should be made aware of this risk in order to provide fast and effective treatment.

**Declarations**

Ethics approval and consent to participate - This study was approved by Poriya Medical Center Institutional Review Board (approval # POR-18-0061)—including analysis of medical records. Need for informed consent was waived by the same Board in the same approval.

Consent to publish—Not applicable

Availability of data and materials—The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. The data is was collected and stored in Hebrew and is courtesy of 2 different Medical Centers, so we’d prefer not to upload it to public repositories.

Competing interests—Not applicable

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Authors’ Contributions - MVJ lead the research team, wrote the IRB approval requests, coordinated data acquiring, coordinated statistical analysis and wrote the manuscript. YG—Proposed the idea, designed the study, co-wrote and edited the manuscript. SZ—Supervised data collection, edited the manuscript. KA—collected and analyzed study data, TZ—collected and analyzed study data, IAEN—contributed to study design, data collection, analyze and interpretation and was a major contributor in writing the manuscript. All authors read and approved the final manuscript

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**Abbreviations**

ANOVA—Analysis of Variance

BUN—Blood Urea Nitrogen

CI—Confidence Interval

ER—Emergency Room

ICD–9—International Classification of Diseases, Ninth Revision

MC—Medical Center

MS—MicroSoft

SD—Standard Deviation

SPSS—Statistical Package for the Social Sciences
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Tables

| Table 1 – Research data and statistic analysis |
|-----------------------------------------------|
|                  | Ramadan | Non Ramadan | p   | 95% CI          |
|------------------|---------|-------------|-----|----------------|
| Total Patients   | 21      | 99          | N/A | N/A             |
| Ratio/month      | 4.2     | 1.8         | 0.001 | 1.46-3.72      |
| Age              | Mean    | 42.88       | 42.88 | 1               |
|                  |         | (-10.09)-10.09 |     |                 |
|                  | SD      | 16.71       | 22.02 |                 |
| Gender           | Male    | 13          | 57   |                 |
|                  | Female  | 8           | 42   |                 |
|                  | M:F ratio | 1.62         | 1.36 | 0.71            |
|                  |         |             |      | 0.52-1.94       |
| Gland            | Parotid | 12          | 58   |                 |
|                  | SM      | 9           | 41   |                 |
|                  | P:SM ratio | 1.28         | 1.4  | 0.86            |
|                  |         |             |      | 0.23-1.95       |
| Leukocytes (*10^9/L) | Mean    | 8.98        | 6.08 | 0.0085          |
|                  |         |             |      | 0.76-5.04       |
|                  | SD      | 2.75        | 4.78 |                 |
| Amylase (U/L)    | Mean    | 360.00      | 370.25 | 0.915        |
|                  |         |             |      | (-200.49)-179.95 |
|                  | SD      | 405.12      | 398.81 |               |
| BUN (mg/dL)      | Mean    | 14.26       | 5.00  | 0.0001          |
|                  |         |             |      | 8.08-10.43      |
|                  | SD      | 3.85        | 2.08  |                 |
| Creatinine (mg/dL) | Mean    | 0.81        | 0.62  | 0.0001          |
|                  |         |             |      | 0.104-0.28      |
|                  | SD      | 0.33        | 0.13  |                 |
| BUN/Cr           | 17.70   | 8.06        | 0.0001 | 2.46-3.28      |

Abbreviations: SD – Standard deviation, SM – Sub-Mandibular, P – Parotid, BUN – Blood Urea Nitrogen, Cr – Creatinine

Figures
Figure 1

The prevalence of sialadenitis during the study