Anaphylactic reactions in adult patients in Southern Israel

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Summary

Background: **Southern Israel is inhabited by Jews and Bedouins. Children from these populations differ in the epidemiology of anaphylactic reactions; however, the effects of ethnicity on the epidemiology of anaphylactic reactions in adults in these populations are unknown.**

Methods: **Retrospective review of medical records of patients with anaphylactic reactions treated in a single institution during 2008-2012.**

Results: **A total of 192 evaluable cases of anaphylaxis were recorded; 155 (80.7%) anaphylactic reactions occurred in Jews and 37/192 (19.3%) occurred in Bedouins. A trend towards an older mean age of occurrence of anaphylaxis was recorded in Jewish patients compared with Bedouin patients: 48.1 years versus 41.2, respectively (*P* = 0.053). Anaphylaxis was more common in Jewish female patients than males and more common in Bedouin male patients than females. Overall, 93/155 (60.0%) females in Jewish patients were affected compared with 14/37 (37.8%) in the Bedouin population (*P* = 0.015). More Jewish patients had more anaphylaxis attributed to food compared with Bedouin patients: 31/155 (20%) versus 2/37 (5.4%) (*P* = 0.034). The mean yearly incidence of anaphylaxis was similar in Bedouin and Jewish patients: 12.1 ± 5.3 versus 17.6 ± 15.3, respectively (*P* = 0.466). However, a significant trend towards a higher incidence of anaphylactic reactions was recorded throughout the study years only in Jewish patients (r = 0.906, *P* = 0.034).**

Conclusions: **Adult Jewish patients have a significantly higher probability of having anaphylactic reactions due to food compared with Bedouin patients, with females being more affected, and the incidence of anaphylactic reaction is increasing only in the Jewish population. The epidemiology of anaphylactic reactions can differ between populations residing in the same geographical area. *(Asian Pac J Allergy Immunol 2016;34:44-50)***

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Introduction

Anaphylactic reactions are severe, systemic and potentially fatal allergic reactions.[1,2] A previous study showed a link between age groups, gender, various geographic and socio-economic conditions in hospitalised patients with anaphylaxis in England.[3] Ethnic and racial disparities associated with anaphylactic reactions have been recorded in Florida.[4] We recently showed that the epidemiology of anaphylactic reactions requiring hospitalisation in southern Israel differs between Bedouin and Jewish children. Significantly more Bedouin children had anaphylactic reactions requiring hospitalisation from hymenoptera stings, possibly from increased exposure to this species, while cow's milk was the main cause in Jewish children.[5]

The Negev region of Southern Israel is a heterogeneously populated area, inhabited by two major populations, Jewish and Moslem Bedouin. The Jewish population lifestyle and standards of living are comparable with those of developed countries, whereas the Bedouin population is still in transition from a semi-nomadic lifestyle to permanent settlement. This population is comparable to that of a developing country. These two populations have access to the same medical services. Medical insurance in Israel is universal and there are no financial barriers to the availability of hospital services in southern Israel. The Soroka

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University Medical Center is the only hospital for the entire region, and all emergency cases are referred to this hospital. Thus, all patients with severe anaphylactic reactions are treated at Soroka University Medical Center.

The purposes of the present study were: to compare the incidence, cause, seasonality, and clinical manifestations of anaphylactic reactions in adults of Jewish and Bedouin populations in Southern Israel and to compare these parameters to the previously published data on anaphylaxis in children from the same area.

Methods

This study was approved by the Soroka University Medical Center ethical committee.

The medical records of all cases of anaphylactic reactions in adults aged 18 years or older from 1 January 2008 until 31 March 2012 were reviewed. Patients with more than one anaphylactic reaction were analysed only once.

The medical records of all adult patients who were either treated at the emergency medicine department or hospitalized with a diagnosis of "anaphylactic shock or reaction" or "allergic reaction" (from any cause) were screened. The diagnosis of anaphylactic reaction was made after a critical review of the medical records by the first and last authors of this manuscript and was based on previously published clinical criteria.[1] Biphasic anaphylactic reactions were recorded only if the medical records showed a recurrence of the initial anaphylactic symptoms during hospitalisation and a clear diagnosis of "biphasic reaction" was recorded in the medical records.

The seasons of the year were defined as follows: winter - December to February, spring - March to May, summer - June to August and autumn - September to November.

In order to calculate the incidence of anaphylactic reactions, we used data published by the Israeli Bureau of Statistics.[6]

Statistical analysis

Differences between Jewish and Bedouin patients, as well as other categorical data, were analysed using the Chi-square test or Fisher exact test, as appropriate. Variations in yearly incidences were studied using linear regression analysis. The proportions of causes and seasonality of anaphylactic reactions from both populations were analysed by t test for proportions. A P value of $\leq$ 0.05 was considered statistically significant.

Table 1. Age and gender data

	Cases N (%)	Average age+/-SD	Gender	
			Male N(%)	Female N(%)
Bedouin	37 (19.3)	41.2± 18.8*	23 (62.2)†	14 (37.8)†
Jewish	155 (80.7)	48.1±19.5*	62 (40)†	93‡ (60.0)†
Total	192	46.8±19.5	85 (44.3)	107 (55.7)

*P (student t-test)=0.053

†P (student t-test)=0.015

‡One Jewish female patient had 2 anaphylactic reactions and was analyzed only once

Result

A total of 193 cases of anaphylaxis were recorded, with one episode occurring twice in the same patient, leaving a total of 192 evaluable episodes of anaphylaxis (Table 1). One hundred and fifty five (80.7%) episodes of anaphylaxis occurred in Jews and 37/192 (19.3%) occurred in Bedouins. A trend towards an older mean age of occurrence of anaphylaxis was recorded in Jewish patients compared with Bedouin patients: 48.1 years versus 41.2, respectively (P = 0.053). Anaphylaxis occurred in 107 female patients (55.7%) and 85 males (44.3%); however, there was a statistically significant difference in gender distribution among Jewish and Bedouin patients: anaphylaxis was more common in Jewish female patients and more common in Bedouin male patients: 93/155 (60.0%) females in Jewish patients compared with 14/37 (37.8%) in the Bedouin population (P = 0.015).

The causes of anaphylaxis differed between Jewish and Bedouin patients, with more Jewish patients having anaphylaxis attributed to food compared with Bedouin patients: 31/155 (20.0%) versus 2/37 (5.4%), respectively (P = 0.034). Medication, hymenoptera stings, or unknown causes were not significantly different between Jewish and Bedouin patients (Table 2). The exact types of foods that were considered to be the cause of anaphylaxis in Jewish patients included fish in 6 patients, Kiwi in 3 patients, peanuts, nuts, peach and wheat in 2 patients each, and persimmon, buckwheat, shrimp and coffee in 1 case each. In 2 patients, anaphylaxis was attributed to candy and spices, with 1 case each, and 8 patients had an anaphylactic reaction attributed to an unidentified food after the simultaneous ingestion of multiple foods. In the 2 Bedouin patients with anaphylactic reactions due to food, one case was

Table 2. Causes of anaphylactic reactions

	Food N (%)	Medication N (%)	Hymenoptera stings* N (%)	Unknown N (%)	Other** N (%)	Total
Bedouin	2 (5.4)	25 (67.6)	3 (8.1)	6 (16.2)	1 (2.7)	37
Jewish	31 (20.0)	83 (53.5)	4 (2.6)	35 (22.6)	2 (1.3)	155
P value***	0.034	0.122	0.132	0.369	0.476	
Total	33 (17.2)	108 (56.3)	7 (3.6)	41 (21.4)	3 (1.6)	192

*In Bedouins- 2 from bees, 1 unknown hymenoptera, in Jews- 2 from bees, 2 from hornets.

** Includes airplane Soap (1 case- occurred twice in one patient), Exercise (one case), shampoo (one case)

*** Chi square test or fisher exact test, as appropriate

attributed to fish and the other occurred after ingestion of a cocoa drink.

Analysis of specific types of medications that were considered to cause anaphylaxis revealed more anaphylaxis due to non-steroidal anti-inflammatory drugs (NSAIDs) in Bedouin patients compared with Jewish patients: 7/25 (28.0%) versus 8/83 (9.6%), respectively (P = 0.042). Other medications, including beta lactam antibiotics, proton pump inhibitors, intravenous radio-contrast, and dipyrone as the cause of anaphylaxis were not significantly different between Bedouin and Jewish patients.

The hospitalisation rate for anaphylaxis did not differ between Bedouin and Jewish patients: 18/37 (48.6%) of the Bedouin patients were hospitalised compared with 67/155 (43.2%) of the Jewish patients (P = 0.551).

The mean yearly incidence of anaphylaxis that was severe enough to warrant a referral to a hospital did not differ between Bedouin and Jewish patients: 12.1 ± 5.3 versus 17.6±15.3, respectively (P = 0.466) (Table 3). However, a significant trend towards a higher incidence of anaphylactic reactions was recorded throughout the study years only in

Table 3. Yearly mean incidence of anaphylactic reaction by ethnicity

year	Bedouin cases N (%)	Jewish cases N (%)	Total cases N	Bedouin population	Jewish population	Total population >=18 years	Bedouin Incidence (/100,000 inhabitants)	Jewish Incidence (/100,000 inhabitants)	Total incidence (/100,000 inhabitants)
2008	9 (24.3)	15 (9.7)	24	63,780	262,560	326,340	14.11	5.7	7.35
2009	7 (18.9)	23 (14.8)	30	79,620	271,220	350,840	8.79	8.48	8.55
2010	4 (10.8)	24 (15.5)	28	84,100	273,540	357,640	4.76	8.77	7.83
2011	13 (35.1)	64 (41.3)	77	88,160	275,880	364,040	14.75	23.2	21.15
2012*	4 (10.8)	29 (18.7)	33	22,040*	68,970*	91,010*	18.15	42.05	36.26
Mean incidence (+/- SD)							12.1 (5.3) †	17.6 (15.3) †	16.2 (11.2)

* The data for 2012 were recorded until 31 March 2012; incidence was calculated relatively for 3 months

† P (Student t-test for comparison between 2 ethnicity populations) >0.05

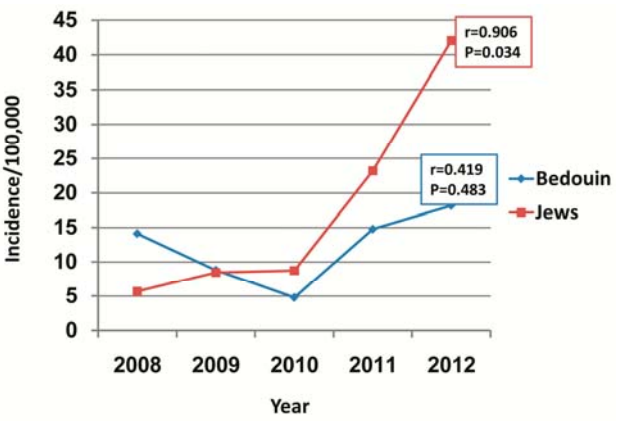

Figure 1. Yearly incidence of anaphylactic reactions in Bedouins and Jews

Jewish patients (r = 0.906, *P* = 0.034 in the Jewish population and *r* = 0.419, *P* = 0.483 in the Bedouin population) (Figure 1). The yearly mean incidence of patients who were hospitalised was also not significantly different between Bedouin and Jewish patients: 4.6 versus 5.8, respectively (*P* = 0.496).

There was no significant seasonal pattern in the occurrence of anaphylactic reactions in the entire study population due to the three major causes of anaphylaxis: food, medications and hymenoptera stings; there was also no seasonal variation between Bedouin and Jewish patients (Table 4).

Biphasic anaphylactic reactions were recorded in 2/37 (5.4%) Bedouin patients compared with 7/155 (4.5%) Jewish patients (*P* = 0.685); four cases occurred during hospitalisation and 5 were in the emergency medicine department. The causes of these reactions were attributed to intravenous radio-contrast, amoxicillin-clavulonate, other medications (2 cases each) and 3 cases due to an unknown cause.

The clinical manifestations of anaphylaxis were similar in Bedouin and Jewish patients. Dermatological manifestations occurred in 36 Bedouin patients (97.3%) compared with 153 (98.7%) Jewish patients; respiratory manifestations: 32 (86.5%) compared with130 (83.9%); haemodynamic manifestations (shock): 11 (29.7%) compared with 36 (23.2%); gastrointestinal manifestation: 5 (13.5%) compared with 13 (8.4%); and neurological manifestations: 4 (10.8%) compared with 23 (14.8%), for Bedouins versus Jewish patients, respectively. All of these differences were found to be non-significant (*P* > 0.05).

Previous anaphylaxis, before the instance that led to inclusion in this study, were recorded in 7/37 (18.9%) Bedouin patients compared with 32/155 (20.6%) Jewish patients (*P* = 0.866). Automatic adrenaline injectors were available in 5/32 (15.6%) of the Jewish patients compared with none of the Bedouin patients (*P* = 0.562). Utilisation of automatic adrenaline injectors was used by only 3 of the Jewish patients. A non-significant trend was recorded towards more treatment with adrenaline by emergency medical services before arrival to the hospital in Bedouin patients: 9/37 (24.3%) Bedouin patients compared with 19/155 (12.3%) Jewish patients (*P* = 0.062). Conversely, there was a non-significant trend towards more frequent treatment with adrenaline in Jewish patients in the hospital 41/155 (26.5%) compared with 5/37 (13.5%) Bedouin patients (*P* = 0.098).

Discussion

This study shows different patterns of anaphylactic reactions in adult patients from two distinct populations residing in the same

Table 4. The seasonality of the major causes of anaphylactic reactions

Season	Food N (%)		Medications N (%)		Stings N (%)		Total N (%)	
	Bedouin	Jewish	Bedouin	Jewish	Bedouin	Jewish	Bedouin	Jewish
Autumn	0	2 (6.5)	4(16)	20(24.1)	0	1(25.0)	4	23
Winter	0	14(45.2)	9(36)	20(24.1)	1 (33.3)	0	10	34
Spring	2 (100)	7 (22.6)	6 (24)	22(26.5)	0	0	8	29
Summer	0	8 (25.8)	6 (24)	21(25.3)	2 (66.7)	3(75.0)	8	32
Total	2*	31*	25†	83†	3‡	4‡	30	118

For the difference in seasonality between Bedouin and Jewish patients:*P >0.05. †P>0.05 (Chi square test or fisher exact test, as appropriate), ‡P=incalculable due to small sample size

For the seasonality of the entire study population:*P=0.152, †P=0.966, ‡P=0.272.

geographical area in Southern Israel. In the Jewish population, the incidence of anaphylactic reaction is rising, is more commonly attributed to food and occurs at an older age compared with the Bedouin population. Previously published data on the epidemiology of anaphylactic reactions requiring hospitalisations in children in Southern Israel from 2005-2010 showed that food, and specifically cow's milk, was a significantly more common cause of anaphylaxis in Jewish children compared with Bedouin children, while hymenoptera stings were more common in Bedouin children as a cause of anaphylaxis.[5] In this study, food was still a more common cause of anaphylaxis in Jewish adult patients; however, none of these patients had cow's milk as the cause of the anaphylaxis and hymenoptera stings did not cause more cases of anaphylaxis in adult Bedouin patients. Although we do not have confirmed research data on the differences in diets between Bedouin and Jewish populations in children or adults in our area, the Bedouin population's diet is usually more traditional, with less dining in restaurants, and the consumption of tropical fruits such as kiwi or sea food. In addition, cooking methods and the consumption of food additives such as preservatives, monosodium glutamate and food colours may also be different between the 2 populations; these possible differences may play a role in the higher rate of anaphylaxis from foods in the Jewish population. Indeed, Katz et al. reported a significantly different exposure to milk in Arab Moslem infants in central Israel (some of them are of Bedouin ethnicity) correlating with a lower incidence of milk allergy in Moslem Arab infants.[7] Although we do not have specific data on maternal feeding habits, the consumption of cow's milk or breast feeding among Bedouin mothers compared with Jewish mothers in our area, if the Bedouins living in southern Israel have similar feeding habits to Arab Moslems in central Israel, this may explain in part the differences in anaphylaxis due to food between Bedouin and Jewish adults in our area.

Anaphylaxis due to medications was similar overall between the Jewish and Bedouin populations, although anaphylaxis from NSAIDs was significantly more common in the Bedouin population. This finding may be due to the increased consumption of NSAIDs in the Bedouin population; however, we do not have specific data on the different NSAID consumptions of these populations.

Our findings are somewhat similar to studies from Florida, with a higher likelihood of African American subjects suffering from anaphylaxis due to food and lower likelihood of anaphylaxis due to stings[4]; similarly, white, non-Hispanic males had a higher likelihood of experiencing anaphylaxis due to venom.[8] This epidemiological pattern may also be true in other distinct populations residing in the same geographical areas across the world.

Throughout the study period, a significant increase in the incidence of anaphylactic reactions was only recorded in the Jewish population. We do not have an explanation for the increase in anaphylaxis incidence only in this population; however, the incidence of anaphylaxis has been reported to be increasing in various locations.[9,10] Future monitoring of the incidence of anaphylactic reactions in this population may reveal whether this trend is consistent and reflects a steady increase.

The incidence of anaphylactic reactions requiring hospitalisations is similar in both Bedouin and Jewish adult patients; however, we have shown that children have a slightly higher incidence of anaphylactic reactions requiring hospitalisation in southern Israel. These differences may be attributed to the slightly different methods utilised in the previous study.[5] The effects of age on the incidence of anaphylaxis have been studied extensively. In a review conducted by the "American College of Allergy, Asthma, and Immunology Epidemiology of anaphylaxis working group" it was concluded "that most incident cases occur among children and adolescent patients."[11] Sheikh and Alves have shown that the highest hospitalisation rate due to anaphylaxis in England occurs between the ages of 15 and 54 years.[3] Harduar-Morano et al. showed two peaks of anaphylaxis incidence calculated by assessing emergency department visits in Florida: in males aged up to 4 years of age and in females aged 15-54 years.[4] A study from Rochester, Minnesota, showed that the highest incidence of anaphylaxis occurs between the ages 0 and 19 years.[12] A study from Brisbane, Australia suggested that paediatric anaphylaxis was less common than anaphylaxis in adults[13] and Simons et al. showed that in Manitoba, Canada, the highest dispensing rate of automatic adrenaline injectors was reported in children aged 12-17 months.[14] These conflicting data may be due to different study methods or definitions; however, we suggest that it is possible that the epidemiology of anaphylaxis indeed varies considerably between

populations and that such variations may exist even in populations residing in the same area.

In adults, anaphylactic reactions are more common in females;[1,3,4] this was also our finding in the Jewish population; however, in the Bedouin population, male patients were affected more often than females. We do not have a good explanation for this finding.

Contrary to the higher rate of anaphylaxis from hymenoptera stings in Bedouin children compared with Jewish children, hymenoptera stings were not found to be significantly more common in Bedouin adults compared to Jewish adults and only a non-significant trend was recorded. We believe that this finding is due to the small sample size. The Bedouin population tends to live in rural areas and spend more time outdoors, possibly allowing for more hymenoptera stings occurring in Bedouins, causing allergic sensitisation.

In other studies, anaphylaxis due to venom or hymenoptera stings has been shown to have a clear seasonal variation, with most cases occurring in July to October.[4,14,15] We did not find a seasonal variation in the occurrence of anaphylactic reactions due to hymenoptera stings, as previously reported;[4,15,16] however, in our study, 5 out of 7 patients suffered from anaphylaxis due to hymenoptera stings during the summer, suggesting that the lack of significance in this study is due to the small sample size. Furthermore, multiple hymenoptera stings in children in southern Israel have been shown to occur almost exclusively in the late summer and early fall.[17]

Only 5 patients had an automatic adrenaline injector available with them at the time of the anaphylactic reaction and only 3 patients actually used their injector. These data suggest that increased awareness of the benefits of having and using an automatic adrenaline injector is required, probably in both physicians and patients.

In general, the Bedouin population lives in areas that are relatively remote from the hospital; this usually causes a delay in arrival to the hospital after a medical emergency and is probably the cause of the trend towards increased adrenaline therapy by emergency medical services prior to arrival at the hospital in Bedouin patients.

The limitations of the present study are related to the retrospective collection of data and the fact that the causes of anaphylactic reaction were determined by analysing the patient medical records at the time of hospitalisation. We do not have data available on the results of skin prick testing, Radio Allergic Sorbent Test (RAST) for specific IgE or controlled challenges for the suspected allergen. Therefore, the causes of anaphylactic reaction, as determined in this study, represent presumed ones and there is a possibility that some cases were due, in fact, to causes other than those recorded.

We conclude that the causes of anaphylactic reactions requiring hospitalisation in southern Israel differ between children and adults. The epidemiology of anaphylactic reactions also differs in Jewish and Bedouin adults in Southern Israel. Adult Jewish patients have a significantly higher probability of experiencing anaphylactic reactions due to foods, are more likely to be female compared with Bedouin patients and the incidence of anaphylactic reaction in the Jewish population is rising. These differences may be relevant to other areas in which more than one ethnicity resides.

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