

A Cross-Sectional Observational Study of Clinical Spectrum and Prevalence of Fixed Food Eruption in a Tertiary Care Hospital

Abstract

Background: Fixed food eruption (FFE) is a rare type of hypersensitivity reaction occurring after ingestion of some food items in the form of recurrent erythematous patches, bullae, vesicle, or pustule at the same site after ingestion of same or related food products. Various items listed responsible for causing FFE include tree nuts, groundnuts, legumes, lentils, eggs, fruits like kiwi, strawberry, tonic water, and tartrazine. Its more commonly reported in developed countries with no Indian studies as of yet. We studied the clinical spectrum and prevalence of FFE in a tertiary care hospital. **Objective:** To study the prevalence and pattern of FFE after eliminating all other possible causes including drug rash. **Materials and Methods:** A cross-section observational study of 27 consecutive patients suspected to have fixed food eruption after eliminating all possibilities of any drug reaction to the best of our knowledge. Informed consent was obtained from the patients, and ethical clearance was taken from the hospital ethical committee. **Results:** A total of 27 patients were studied out of which 18 (66.66%) were females and 9 (33.33%) were males. The prevalence of fixed food eruption was calculated to be 0.072%. Fixed food eruption was noted secondary to cashew nuts (14.8%), almonds (7.4%), walnut (7.4%), pistachio (3.7%), strawberry (3.7%), kiwi (3.7%), and cheese crisps (3.7%). **Conclusion:** This observational study highlights the varied patterns of fixed food eruptions as well as the burden of disease in population secondary to certain diets.

Keywords: Fixed food eruption, Indian population, open oral challenge test, prevalence

Introduction

In 1984, the term erythematous pigmented fixed eruption was first coined by Brocq. He described a characteristic eruption induced by antipyrine. Since then, it has been termed fixed drug eruption caused by re-exposure to the same drug.^[1] Fixed food eruption (FFE) is a benign recurrent skin hypersensitivity reaction that tends to recur at the previously involved sites following re-exposure to the offending food item. It bears analogy to fixed drug eruptions which present as erythematous, single or multiple patches or plaques on re-exposure to the inciting drug and usually resolve with post-inflammatory hyperpigmentation.^[2] English literature quotes a list of around 10 food items as potential triggers for FFE. These include cheese crisps, strawberries, lentils, lactose-containing medicines and food items, asparagus, tonic water, quinolone yellow dye, cashew-nuts, Japanese sand lance, seafood (shell-fish, crabs, squids, and shrimps), and peanuts.^[2-11] The pathophysiology of FFE is thought to

be multifactorial in origin. The typical rash of FFE is erythematous to dusky violaceous in nature arising on any site of the body usually within 12–24 h of food exposure. This implies that FFE can occur along with IgE-mediated symptoms.^[7,12] It is shown that the pathomechanisms involved may be similar to that of fixed drug eruption where memory CD8+ T cells specific to drug reside and persist in the skin. These are reactivated on re-exposure to drug and mediate keratinocytes apoptosis, which results in the typical cutaneous lesion.^[13]

Materials and Methods

This was a cross-sectional observational study carried out in a tertiary care hospital in India for a duration of 1 year from May 2018 to May 2019. A sample size of 27 was calculated based upon the prevalence of FFE of western literature, as no studies were available from India on literature search. A pilot study conducted in European country revealed prevalence as 8%. The

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sample size of study was calculated using the absolute precision method.

$$n = Z_{(1-\alpha/2)}^2/d$$

Where: n = sample size required for one arm

$1-\alpha/2$ = standard normal variate (at 5% type 1 error, $P < 0.05$, it is 1.96). As in the majority of studies, “p” values were considered significant below 0.05; hence, 1.96 was used in the formula.

d = absolute precision (margin of error), 0.1.

Using the above formula, sample size of 27 was calculated. Twenty-seven consecutive patients visiting skin OPD directly as well as referred from hospitals across country and suspected of FFE were recruited in the study after obtaining informal consent from the patients and guardians and meeting the inclusion criteria (history of recurrent rash occurring at the same site within 30 min to 24 h of consumption of a food item and excluding other causes like drugs and photo exposure). Ethical clearance was obtained from the hospital ethical committee. Patients were divided into categories depending on their age groups ranging from 1 to 70 years of age. Food items under study were as follows: cashew nut, almond, walnut, pistachio, pignolia nut, hazelnut, brazilnut, Macedonia nut, groundnut, peanut, seafood including shellfish; crab; squid; and shrimp, asparagus, strawberry, kiwi, cheese crisps, lactose-containing food, tonic water, tartrazine, and lentils. A complete history of all the food items was taken and any case of drug intake within the past 8 weeks was ruled out to the best of our knowledge. Skin biopsy was done for histopathology confirmation wherever needed. Confirmation of food eruption in patients was done by conducting patch tests using the suspected food item and admixing in 30% petrolatum. The suspected food items in the vehicle were applied at the site of the eruption as well as the unaffected site in the proximity to reproduce the fixed lesion. Oral challenge test was also done for patients with food eruption after taking their consent.

Procedure for performing oral challenge test

Oral food challenge test is an unmasked, unblinded test that includes feeding a food item in its natural form. This test is conducted when objective symptoms are expected and there is low concern for bias. It is a form of office setup challenge procedure in which a simplified protocol of age-appropriate serving of the suspected food items is fed to the patient gradually. This is followed by an observation of about 1–2 h. However, it has a high potential for bias, which is the main limitation of this test. Although a negative oral challenge test openly rules out any reaction to food items, the positive test further need to be confirmed by a blinded oral food challenge test. In our study, open oral food challenge test procedure was used as it is cost-effective and saves resources and time. Another reason

is that only one-third of the food challenge tests result in positive results; it was thus considered to be our first and reasonable choice of evaluating an adverse reaction to food. Dosing schedule for open oral challenge test is listed in [Table 1]. In our study, 3 patients did not volunteer for oral challenge test. Photographs were taken. Data were recorded on Microsoft excel sheet and descriptive analysis was done using SPSS software.

Results

A total of 27 patients out of the total of 35, 500 patients presenting to the Dermatology OPD of tertiary care hospital were diagnosed as a case of FFE [Figures 1 and 2]. The prevalence of FFE was calculated to be 0.072%. Of these, 18 (66.66%) were females and 9 (33.33%) were males. The age of these patients ranged from less than 10 years of age to 70 years of age [Table 2]. FFE was noted as follows: cashew nut 4 (14.8%), groundnut 3 (11.1%), almond 2 (7.4%), walnut 2 (7.4%), pistachio 1 (3.7%), hazelnut 1 (3.7%), shellfish 2 (7.4%), crab 2 (7.4%), squid 1 (3.7%) strawberry, kiwi, eggs and cheese crisps each 1 (3.7%), tartrazine 3 (11.1%), and lentils 2 (7.4%). There were no eruptions noted for asparagus, pignolia nut, Brazil nut, Macedonia nut, shrimps, and lactose-containing food or tonic water under the present study [Table 3]. Oral challenge test was negative in patients having eruptions because of cooked lentils. It was confirmed by food elimination and history taking [Table 4].

The various patterns of FFE observed were bullous 10 (37.03%), exanthematous and urticarial each 7 (25.92%), vesicular 2 (7.4%), and pustular 1 (3.7%) [Figure 3a-d]. Majority of FFEs were observed on trunk 6 (22.2%) followed by face 5 (18.5%), oral and genital mucosa each 4 (14.8%), upper limb 4 (14.8%), and lower limb 4 (14.8%) [Tables 5 and 6].

Discussion

FFE and allergies to plants are most commonly seen and studied in the European population. The overall prevalence of FFE in European countries is around 8%.^[14] In our study, the prevalence was found to be around 0.072%, which is very less as compared to that seen in western literature.

Table 1: Dosing schedule for open oral challenge test

Food item	Quantity/portion size
Egg	1 hard boiled or scrambled egg
Shellfish	2-3 oz cooked shell fish
Crab	2-3 oz cooked crab
Squid	2-3 oz cooked squid
Peanut	30 gm/2 tablespoon of peanut butter
Treenuts (cashewnut, almonds, pistachio, walnut)	30-40 gm of crushed nuts/25-30 pieces
Fruits	½ to 1 cup of raw/canned/cooked fruits or 6-8 oz of fruit juice



Figure 1: Fixed food eruption to cashew nut

A probable explanation could be early exposure of infants and children to the surrounding environment as explained by farm effect and hygiene hypothesis. Another explanation for varying patterns of food eruptions and allergies in different geographic regions is different dietary habits and sensitization to food items. FFE is seen commonly for tree nuts like hazelnut and pignolia nuts, which are more commonly seen in European countries: walnut and cashew nut in USA and Brazil nut and almonds in UK. Eruptions with hazelnut were reported in six out of seven studies conducted in Europe. The estimated prevalence was 17–100% of all the other tree nuts.

Another two studies were reported from USA, according to which walnut and cashew were the leading cause of FFE with a prevalence of 20% to 30% for being estimated for walnut and 15%–30% for cashew nut. One study conducted in Mexico reported overall prevalence because of tree nuts being 0.18%.^[14] In countries like India where these plants are not grown, nil cases were observed in our study. In our study, prevalence for the fixed food eruption was found to be highest for cashew nut 4 (14.8%) followed by almond 2 (7.4%), walnut 1 (3.7%), pistachio 1 (3.7%), and hazelnut 1 (3.7%) in that order. Cross reaction was also seen to almonds in one case of FFE with cashew nut, which was confirmed on doing oral challenge test with both food items individually leading to food eruption at the same



Figure 2: Fixed food eruption to shell fish

site again. Patch test was found positive at the affected site and negative at non-affected site for all tree nuts and groundnuts. In our study, an interesting case of FFE was noted after consumption of “nutella” in a child of 6 years of age. The patient presented with an erythematous rash over trunk, which was persisting at the same site. After taking thorough drug history and exposure to any irritant, food history was elicited. The patient admitted consuming nutella with bread every morning in breakfast from the past 1 month. The contents of nutella were studied, hazelnut with cocoa was found to be the main constituent. Oral challenge test was performed with hazelnut to confirm the diagnosis that lead to reduplication of rash at the same site. The patient was counseled and advised to avoid consuming hazelnut in the form of nutella or raw whole nut. Du Toit *et al.* have hypothesized in their study regarding variations in the pattern of peanut allergy seen between populations in UK and Israel, which are genetically similar.^[15] This could be explained due to the difference in consumption of peanuts in infancy and early childhood. There has been an argument that food eruption also varies with consumption of boiled versus roasted peanuts. However, in our study, the two cases of peanut FFE were seen after the consumption of roasted peanuts.^[16,17]

In our study, three cases were noted of FFE secondary to tartrazine. These three cases were found to be positive for a

Table 2: Age distribution of fixed food eruption

Age category	Males	Females	Total	Percentage
1-9 years	3	4	7	25.9
10-19 years	2	3	5	18.5
20-29 years	1	2	3	11.1
30-39 years	1	2	3	11.1
40-49 years	2	2	4	14.8
50-59 years	1	2	3	11.1
60-70 years	0	2	2	7.4
Total	9	18	27	

Table 3: Prevalence of fixed food eruption to various food items

Food items	Total number	Percentage
Cashew nuts	4	14.8
Almonds	2	7.4
Pistachio	1	3.7
Pignolia nut	0	0
Hazel nut	1	3.7
Macedonia nut	0	0
Brazil nut	0	0
Walnut	2	7.4
Groundnut	3	11.1
Shell fish	2	7.4
Crab	2	7.4
Squid	1	3.7
Shrimp	0	0
Asparagus	0	0
Strawberry	1	3.7
Kiwi	1	3.7
Cheese crisps	1	3.7
Lactose	0	0
Tonic water	0	0
Tartrazine	3	11.1
Lentils	2	7.4
Eggs	1	3.7

patch test at the affected site. It was found to be negative at the nonaffected site. Oral challenge test was not conducted as the patients did not consent for it. Few studies have been conducted on tartrazine as a potential agent for causing FFE. These agents contain inoline cores that structurally show resemblance to fluoroquinolone antibiotics. This agent is widely used as a preservative in food items and is considered to be a dye used in the preparation of food items. Cross-reactivity with aspirin is also reported in a few case reports. Cheese crisps are also known to contain tartrazine. It is, therefore, very difficult to pin down the exact cause of FFE to be tartrazine or the drug-containing it as a dye.^[11,18] Fixed eruptions to tartrazine are often challenging to identify as the source is not always a food item. These cases require a thorough history taking for intake of any food containing additive or any recent intake of drug-containing tartrazine as one of its constituents. Our cases were, however, confirmed by patch tests and were

Table 4: Diagnosis of fixed food eruption to various food items

Food items	Oral provocation test	Patch test over affected site	Patch test over unaffected site
Cashew nuts	+	+	-
Almonds	+	+	-
Pistachio	+	+	-
Pignolia nut	NA (not applicable)	NA	NA
Hazel nut	+	+	-
Macedonia nut	NA	NA	NA
Brazil nut	NA	NA	NA
Walnut	+	ND	ND
Groundnut	+	ND	ND
Shell fish	+	+	-
Crab	+	+	-
Squid	+	+	-
Eggs	+	+	-
Shrimp	+	+	-
Asparagus	NA (not applicable)	NA	NA
Strawberry	+	+	-
Kiwi	+	+	-
Cheese crisps	+	ND	ND
Lactose	NA (not applicable)	NA	NA
Tonic water	NA (not applicable)	NA	NA
Tartrazine	ND	+	-
Lentils	-	ND	ND

NA - Not applicable, ND - Not done

treated with a short course of oral and topical steroids after patient counseling.

Among fruits, one case of FFE secondary to strawberry and kiwi each was noted in our study. Only a few case reports of fixed eruption due to kiwi fruits or kiwi leaves have been described in literature. Our case was confirmed by doing a patch test and oral challenge test. After half hour of oral challenge test with kiwi fruit, patient developed itching and burning sensation around the perioral region. Patch test was found to be positive at the affected site and negative on the non-affected site. In our study, the FFEs were followed by local symptoms like redness, itching, burning, and tenderness at the site. There were few reported constitutional symptoms of low-grade fever, malaise, joint pain, and weakness. There were nil cases of shortness of breath, constriction of chest, hypotension, etc.^[19]

Conclusion

FFE are a rare cause of hypersensitivity to food items. A high index of suspicion is required for the diagnosis, but it should be included as a differential diagnosis when there is a case of persisting and recurring lesion over the same site after intake of related food items. Management includes avoidance of the offending food strictly. Symptomatic treatment with antihistamines and corticosteroids is required on case to case basis. In serious cases where FEE is associated with



Figure 3: Patterns of fixed food eruption. (a) Urticarial. (b) Exanthematous. (c) Bullous. (d) Pustular

Table 5: Pattern of fixed food eruption

Pattern	Number	Percentage
Bullous	10	37.03
Urticarial	7	25.92
Vesicular	2	7.4
Pustular	1	3.7
Exanthematous	7	25.92

Table 6: Site of fixed food eruption

Site	Number	Percentage
Face	5	18.5
Oral mucosa	4	14.8
Genital mucosa	4	14.8
Trunk	6	22.2
Upper limb	4	14.8
Lower limb	4	14.8

anaphylactic symptoms, use of epinephrine is recommended. A detail and comprehensive knowledge on the prevalence of clinical pattern will help in better understanding of the subject. Further studies are needed in developing countries like India about regional variation and time trends of fixed food eruption.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Brocq L. Eruption erythematopigmentée fixe due à l'antipyrine. *Ann Dermatol Venerol* 1894;5:308-13.
2. Kelso JM. Fixed food eruption. *J Am Acad Dermatol* 1996;35:638-9.
3. Fukushima S, Kidou M, Ihn H. Fixed food eruption caused by cashew nut. *Allergol Int* 2008;57:285-7.
4. Waton J, Splingard B, Barbaud A. A new entity: The neutrophilic fixed food eruption. *Contact Dermatitis* 2011;65:44-7.
5. Yanguas I, Oleaga J, González-Güemes M, Goday J, Soloeta R. Fixed food eruption caused by lentils. *J Am Acad Dermatol* 1998;38:640-1.
6. Tsuruta D, Sowa J, Kobayashi H, Ishii M. Fixed food eruption caused by lactose identified after oral administration of four unrelated drugs. *J Am Acad Dermatol* 2005;52:370-1.
7. Volz T, Berner D, Weigert C, Rocken M, Biedermann T. Fixed food eruption caused by asparagus. *J Allergy Clin Immunol* 2005;116:1390-2.
8. Muso Y, Kentarou O, Itami S, Yoshikawa K. Fixed eruption due to quinine: Report of two cases. *J Dermatol* 2007;34:385-6.
9. Tsuruta D, Sowa J, Kobayashi H, Ishii M. Fixed food eruption caused by Japanese sand lance. *J Clin Exp Dermatol* 2009;34:309-10.
10. Leleu C, Boulitrop C, Bel B, Jeudy G, Vabres P, Collet E. Quinoline Yellow dye-induced fixed food-and-drug eruption. *Contact Dermatitis* 2013;68:187-8.
11. Sohn K, Kim B, Kim J, Song W, Kang H, Park H, et al. Fixed food eruption caused by *Actinidia argente* (Hardy Kiwi): A case report and literature review. *Allergy Asthma Immunol Res* 2017;9:182-4.
12. Parker A, Pinson M, Wohltmann W, Gomez R. Fixed food eruption caused by peanut and cashew: A case report and review of the literature. *J Allergy Clin Immunol Pract* 2015;3:119-22.
13. McWilliam V, Koplin J, Lodge C, Tang M, Dharmage S, Allen K. The prevalence of tree nut allergy: A systematic review. *Curr Allergy Asthma Rep* 2015;15:1-13.
14. Du Toit G, Katz Y, Sasieni P, Mesher D, Maleki S, Fisher H, et al. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. *J Clin Exp Dermatol* 2008;122:984-91.
15. Beyer K, Morrow E, Li X, Bardina L, Bannon G, Burks A, et al. Effects of cooking methods on peanut allergenicity. *J Clin Exp Dermatol* 2001;107:1077-81.
16. Turner P, Mehr S, Sayers R, Wong M, Shamji M, Campbell D, et al. Loss of allergenic proteins during boiling explains tolerance to boiled peanut in peanut allergy. *J Clin Exp Dermatol*

- 2014;134:751-3.
17. Orchard D, Varigos G. Fixed drug eruption to tartrazine. *Australas J Dermatol* 1997;38:212-4.
 18. Grzelewska-Rzymowska I, Szmidt M, Kowalski ML, Rozniecki J. Sensitivity and tolerance to tartrazine in aspirin-sensitive asthmatics. *AllergoImmunopathol (Madr)* 1986;14:31-6.
 19. Taylor SL, Hefle SL, Binsley JC. A consensus protocol for the determination of threshold doses of the allergenic food: How much is too much? *Clin Exp Allergy* 2004;34:689-95.