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ABSTRACT

***Background*:** Cashew nut allergy is a significant tree nut allergy that is increasing gradually and becoming serious health issue these days. Allergens responsible for cashew nut allergy are highly potent and for some people, these reactions have the potential to be severe and even life-threatening (anaphylaxis). Increased consumption of cashew nuts and a change in eating and cooking may be responsible. It's time to spread the knowledge and awareness about cashew nut allergy among society, clinics and development of clinical confession.

Scope and approach: In recent era, various researches regarding cashew nut allergy are under consideration. In this comprehensive review, investigations were carried to identify aspects of cashew nut allergy including its prevalence, characteristics, processing effects, different allergens, diagnosis and management.

***Key findings and conclusion*:** Main etiology is the utilization of minor quantity of cashew nut allergens like Ana-o-3, Ana-o-1 and Ana-o-2, proposed to be very powerful as compared to other tree nuts. Its prevalence is increasing especially in children. Several methods like oral immunotherapy, adrenaline auto-injector device and enzymatic processing are very helpful in the treatment of this emerging type of allergy. Moreover, labelling of foods products having cashew nuts plays significant role in prevention of cashew nut allergy. This information concludes that allergen of cashew nut allergy may be powerful that is chronic cause of many immune disorders.

Key words: cashew nuts, allergy, allergens, oral immunotherapy, hypersensitivity

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1. BACKGROUND

Allergic reactions are ranged from insignificance skin symptoms to anaphylactic shock and resulted in about 200,000 emergency regions visits annually (Clark et al., 2011). These are caused by various foods. Proteins in these foods are the components responsible to stimulate the allergic reactions and are present in three different forms i.e. primary, secondary and tertiary proteins. Allergic reactions are owing to single peculiar food (i.e. if allergy is due to a single type of protein found in eatables e.g. peanut or egg) or multi foods (i.e. if allergy is due to one or more than one protein in more than one food). Proteins that are exploited in the processing of food are derived from different sources. They are estimated to be grouped in gelatin that are animal proteins and milk proteins that are derived from animals (Penny, 1999). Indeed, vegetable proteins are comparatively economic and easily available in market than other proteins. These proteins show immense prospective as direct food for the utilization of humans. Tree nuts and peanuts are responsible for intense stern complications and reactions and occupy the majority of fatal food-induced reactions (Bock, Furlong & Sampson**,** 2007).

Tree nut allergy is common and often severe. It has become an important heal concern as availability and consumption increased. The prevalence of this type of allergy varies by age and geographic region and appears to have increased in children. Accidental ingestion of tree nuts is common. Tree nuts allergy reactions range from mild itching of the mouth to anaphylaxis. It accounts for 18-40 % of cases of anaphylaxis (Weinberger & Sicherer, 2018). In a report presented by American Heart Association dietary metrics, nuts are the most important components for promoting health and aid in decreasing the rate of various diseases for 2020 (Jones et al., 2010).

Especially in pine nut, the pattern of fatty acid composition proved to have advantages because of the minimum saturated fatty acid substances and maximum unsaturated fatty acids. Linoleic acid is present abundantly in pine nuts and these are proved to exhibit advantageous consequences on blood lipids, blood pressure, and serum cholesterol (Nergiz & Donmez, 2004). Although for two decades or more the peanut allergy has been going to increase, recent studies and researches point out that cashew nut is considering as important type of food allergen (Hourihane et al., 2001; Rance, Bidat, Bourrier & Sabouraud, 2003).

The rapid proliferation in the utilization of cashew nuts and the alteration in cooking and eating traditions are dependable due to rapid increase in consequences of cashew nut allergy (Rance, Bidat, Bourrier & Sabouraud, 2003). Inoue et al. (2018) reported that cashew nuts are capable of causing severe allergic reaction. There has been an increasing trend of cashew nut allergies in whole world especially Singapore (Chitta et al., 2018). In a study, Van der Valk et al. (2014) testified that the prevalence of cashew nut allergy is increasing day by day but the level of evidence for this is low. This allergy involves severe reactions including anaphylaxis. But it is clearly an underestimated important healthcare problem especially in children.

1.1. Cashew Nuts

Cashew nut, *Anacardium occidentale* L., belongs to the Anacardiaceae family and is an evergreen tree native from northeast region of Brazil which expanded spontaneously in South American countries (Asogwa et al., 2008). In almost sixteenth century, cashew nuts are dig in Portugal in northeastern part and in count, the cashew nut trees are also circulated in other region of the world (Ologunde et al., 2011). Cashews are the third most consumed tree nut in the United States (Mah et al., 2017). Among tree nuts, cashew nuts rank third in worldwide production (kernel basis), with a world average production of 547,371 metric tons (kernel basis) in the last 10 years with a continuous raising trend. Cashew trees can grow from sea level to an altitude of 1000 m. the tree produces a soft, shiny, and juicy fruit known as cashew apple which bears a single-seeded nut in its bottom covered with a hard gray shell.

Cashew nut (*Anacardium occidentale* L.) kernels are regarded as a nutritious food product, worldwide. The kernels of cashew nuts are externally covered with a thin and reddish-brown-coloured skin, known as testa. The testa constitutes about 1–3% of the total weight of cashew nuts and is found to provide a rich source of hydrolysable tannins with polymeric proanthocyanidins as major polyphenols (Trox et al., 2011). In general, the predominant phenolic acids identified in cashew skin are syringic, gallic, and p-coumaric acids. High temperature (HT)-treated (130 °C for 33 min) cashew skin demonstrated 3-fold higher gallic acid compared to raw cashew, suggesting the release of gallic acid during heat processing. The skin of cashew contains higher amounts of hydrolysable tannins, catechin, epicatechin, and epigallocatechin than raw cashew.

Thus, it is possible that roasting may yield gallic acid from hydrolysable tannins present, leading to its higher content in roasted skin. The HT-treated cashew skin had a higher TPC and antioxidant activity than the low-temperature-treated (70 °C for 6 h) samples. In general, HT-treated skin had a higher flavonoid content, which demonstrated a significant increase compared to the raw skin. The results obtained by HPLC analysis confirmed the liberation

and isomerisation of these compounds during heat treatment of cashew skin. This further lends support to the significant decrease in tannin content in HT treated cashew skin. More research should be carried out to determine the flavonoids content of cashew co-products.

As per nutritional characterization, it is noted that the roasting processes had some effect on moisture, protein, phospholipids, sugars, and certain minerals. All the types of the cashews were found to contain bioactive compounds including oleic acid, linoleic acid, phytosterols, arginine, tocopherols, magnesium, and phenolic compounds. Of the three varieties, the wrapped nuts had the highest concentrations of phenolics and tocopherols, due to the presence of the skins. The concentrations of phytosterols in all of the cashew varieties were higher than reported values for other nuts (Griffin & Dean, 2017).

The raw cashew nut kernels were found to possess appreciable levels of certain bioactive compounds such as β-carotene, lutein, zeaxanthin, α-tocopherol, γ-tocopherol, thiamin, stearic acid, oleic acid, and linoleic acid. Whereas the Flores hand-cracking method exhibited similar levels of carotenoids, thiamin, and unsaturated fatty acids in cashew nuts when compared to raw unprocessed samples (Jennifer et al., 2010). These products were found to contain bioactive compounds including mono- and poly-unsaturated fatty acids, phytosterols, arginine, magnesium, tocopherols, and phenolic compounds. All the types of cashews exhibited higher levels of phytosterols than the amounts reported for other tree nuts (Griffin & Dean, 2017).

Generally, cashew nut considered as a nut is not a nut but a seed. Cashew nut is cultured on the edge of the cashew apple and its shape and structure is just like kidney. Cashew nut is surrounded by a covering which has layers of harmful oil. Due to the presence of noxious oil, the cashew is to be baked before eating. The structural design of cashew tree proves it to be a leading tree crop for retrieving area of land. The productivity of the plant can also be increased by thwarting the cutting of forests and inhibiting soil erosion. The substantial importance is shown by cashew tree due to the presence of various components of large economic value.

The role of nuts is vital in nutrition of different civilizations and societies for eras and is basically because of maximum energy, nutritive significance, and different inimitable flavor. It is also examined that nuts are used to recover psychological problems (Carey, Poulose, & Hale, 2012; Herbison et al., 2012), to improve mineral density in bones (Rivas et al., 2013) also lower the rate of depression (Sanhueza, Ryan & Foxcroft, 2013). Nuts played an important role in diets of many cultures and civilizations for centuries due to its high energy and nutritional value as well as its huge variety of flavors and unique taste. Furthermore,

consumption of tree nuts had been linked with several health benefits during the last years due to its particular nutritional composition. Tree nuts are known to contain a high content of unsaturated fatty acids, both mono and polyunsaturated fatty acids, combined with a huge variety of vitamins, minerals, amino acids, phytosterols and generous content of fiber. Consumption of nuts incorporated in a healthy diet was associated not only to a reduced risk of cardiovascular disease and mortality, especially in case of stroke, but also to decreased risk of metabolic syndrome, diabetes, mental health, depression, weight gain and obesity (Kris-Etherton et al., 2008; Ros et al., 2010; Estruch et al., 2013; Fernandez-Montero et al., 2013; Mitjavila et al., 2013; Kendall et al., 2011; Carey et al., 2012; Herbison et al., 2012; Rivas et al., 2013; Sanhueza et al., 2013; Bes-Rastrollo et al., 2009).

Cashew trees are widely spread over tropical areas close to the equator; therefore, the nutritional composition of cashew nuts may vary by origin. Cashew nuts are the source of unsaturated fatty acids, vitamins, fibers, sterols and amino acids wherever it is grown. As far as the bioactive compounds of cashew nuts are concerned, cashew nuts have beta carotene, lutein, zeaxanthin, alpha-tocopherol, gama-tocopherol, thiamin, stearic acid, oleic acid and linoleic acid (Trox et al., 2010). Their injection are important and prove to be beneficial in reference to health (Rico, Bullo & Salvado, 2016). Cashews are associated with reduced cardiovascular disease risk because these are abundant with monounsaturated fatty acids and polyunsaturated fatty acids (Mah et al., 2017).

The cashew fruit possesses maximum nutrient value, nourishing fats and also substantial quantity of vitamins, amino acids, sterols and minerals that exhibits healthy and advantageous consequences on physical condition (Gupta & Prakash, 2014; Ras, Geleijnse & Trautwein, 2014; Blais et al., 2015). Cashews nuts also have antioxidants such as anacardic acids which are alkyl phenols (Medeiros-Linard et al., 2018). The recent research has exhibited that the powdered milk is utilized in the manufacturing of standard recipe of milk chocolate and can be substituted with about 25% roasted cashew kernel (Ogunwolu & Akinwale, 2003). Cashew nuts are main constituent in many processed foods including confectionery products, butters and bakery products and use as a main ingredient in snacks. Cashew apple possesses a constituent that exhibits an important role in the production of cashew kernels, spirits and the cashew beverages shows great importance because of having oil approximately 40-57% and protein content about 21% (Fetuga, Babatunde, Ekpenyong & Oyenuga, 1975). Due to having the characteristics of frailty, they are used in adding sweetness in the desserts.

Cashew nut is use in many countries particularly in Indian cuisines, Chinese and Thai. In the ranking of worldwide edifice of edible nuts, the cashew nut comes at 3rd number and the

main exporters of cashew nuts are Vietnam, India, Brazil and Nigeria considered. On plantation scale, the farming of cashew nut is not planned, in those countries which produce cashew nut in bulk. A very powerful labour is required for the handling of cashew nut, followed by the conversion of raw nut to edible cashew nut, therefore the price of cashew nut is greater than peanuts and other nuts. In world, the production of cashew nut is increasing very rapidly. The production of cashew nut increase about tenfold in previous 50 years. A remarkable difference has been seen in the development of cashew nut, in 2010 the production was improved approximately 3.58 million tonnes in 2010 (Ali and Judge, 2001). Although being the third most produced nut worldwide, to date, very little research has been made on cashews.

2. Epidemiology

It is difficult for food allergens to develop the occurrence and dominance due to different reasons. It is reported that about 170 foods are the main cause of IgE-mediated reactions. However, the foremost consequences are intensive on the most communal eatables. In the occurrence and different consequences of food allergens changes had been observed over time. Indeed, different reports are observing to be potent in raising the consequences in the past 10 to 20 years (Branum & Lukacs, 2009).

Different reports about food allergens in reference to occurrence, consequences, and natural history becomes problematic in comparison because of the irregularity and insufficiency according to the recent definition of food allergens. Generally, many diverse reports show the consequences related to the tree nut allergy. The most common tree nut allergy is said to be the allergy from cashew nuts, however the significance of cashew nut allergy is of great importance (Sicherer et al., 2001). The reports reveal that cashew nut allergy is found in infants to greater extent and in clinical practice there is an increased recognition of cashew nut allergy (Rance, Bidat, Bourrier & Sabouraud, 2003; Davoren & Peake, 2005). In a study, it was revealed that approximately 0.08% of infants less than 4 years in the United Kingdom were reported to be health compromised and sensitized because of cashew nuts (Tariq et al., 1996). Hasegawa et al. (2009) observed relatively more cashew nut allergy in female adults. The study of York et al. (2011) indicates that cashew nut allergy may be more prevalent in the Asian population.

It is also examined that approximately 41% of the individuals with nut allergy in France are found to be sensitive in reference to cashew nut (Vautrin et al., 1998). Comparative increase percentage of cashew nut allergy was examined in adult females (Hasegawa et al., 2009). Another study reveals that cashew nut allergy exhibits a variety of consequences in the

Asian people (York, Dunbar & Luyt, 2007). Out of 100, about 41 individuals are consequent from the multicultural pediatric allergy clinic in Leicester (UK) having medical record that suggests the presence of cashew nut allergy is inherited from either Asian British or Asian background in combination with approximately 21% individuals in reference to the history indicative of allergy to other nuts. Due to the dietary intake the Asian infants have earlier exposure to cashew nuts in contrast to the other populations worldwide. Instead of the increasing impacts exhibited by cashew nuts sensitization and clinical allergy, methodologically and rigorous studies the documentation is not yet been displayed.

The plants of *Anacardiacea* family are responsible for urushiol dermatitis and also a cause of systemic dermatitis and serious allergic interaction dermatitis. Cashew nut is surrounded by a shell and urushiol having ancardic and cardol acid, which is found in cashew nut shell oil. About 57 individuals which have allergy from cashew nut develop a poison ivy-like dermatitis in 1 to 8 days after the intake of cashew nut contaminated by shell oil. Four had rectal itching, three had burning of the mouth, and nine who responded to the cashew extract also responded to poison urushiol. In previous years, the risk of anaphylaxis is increasing, due to increase in the number of those children who had cashew nut allergy. Author suggested that in this case after liver transplantation, hypersensitivity may occur due to the transfer of IgE-mediated with possibly severe significances (Phan et al., 2003).

3. Allergens Present in Cashew Nuts

The clinical significance in reference to nuts of cashew sensitization is maximum because ingesting the nuts instigate various allergic diseases. A competitive inhibition test is use to confirm the presence of cashew allergen in an individual (Valk et al., 2016). The expression allergy and allergic disease generally comprehend and the medical situations are concerned with modified immunologic reactivity. They can either be Immunoglobulin E (IgE) mediated or non- Immunoglobulin E (non IgE) mediated. Immunoglobulin E mediated is defined as the exceptional group of immunoglobulins that are mediated by the proximate reactions of allergy (Clark et al., 2011).

Ana o 1, a vicilin; Ana o 2, a legumin-like 11S globulin; and Ana o 3, a 2S albumin, are well known cashew nut allergens. The Ana o 1 has resistance to heat and proteolysis (Robotham et al., 2005). These are categorized as seed storage proteins. Western immunoblotting checked the cashew nut allergic patients, 81% are allergic to recombinant Ana o 3, 62% to recombinant Ana o 2 and 50% are allergic to recombinant Ana o 1. Sensitization to Ana o 3 is the best predictor of clinical allergy. The cashew nut allergy has been reported second most prevalent tree nut allergy in United States, after walnut allergy.

They are responsible to increase the pervasiveness of cashew allergy especially in infants (Rance, Bidat, Bourrier & Sabouraud, 2003; Hourihane et al., 2001).

The IgE-binding proteins for example 30 kDa & 44 kDa proteins are able to identify with the help of IgE-immuno blot in protein extracts of these nuts (Asero et al., 2014). It is also observed for the characterization, purification and identification of the IgE-binding proteins. The specificity of the IgE targets may be focused by the examination and utilization of particular antibodies (Zienkiewicz et al., 2015). Hypoallergenic and immunogenic are responsible for the production of protein allergens and is the primary approach in emerging the immunotherapy elements because of the allergies aided by IgE. Extensive work is performed on influencing the various allergens in combination of recombinant DNA technology. For instance, the location based mutations due to allergens are responsible for destruction of IgE-combining characteristics. They are also responsible for preserving T-cell epitopes that are the major cause of allergy.

From the extract of soluble proteins, the defatted cashew nut flour is manufactured (Sathe et al., 1997). The amount of proteins can be estimated by the use of the Bradford protein assay (BioRad Laboratories, Inc, Hercules, Calif), in combination of the standard protein such as BSA. The effectiveness of pyrrole-2-carboxaldehyde salicylhydrazone (PCSH) that is used in the immunotherapy for the allergy of cashew can be estimated by lowering the reaction of IgE and preserving T cell enhancing capabilities due to the presence of simple pepsin digestion. Pyrrole-2-carboxaldehyde salicylhydrazone is responsible for the cure of cashew allergy which is mediated by pyrrole-2-carboxaldehyde salicylhydrazone immunotherapy. It works with effectiveness as performed by native cashew proteins (nCSH) immunotherapy. It allows lowering the allergic reactions on contest with native cashew proteins. Pyrrole-2-carboxaldehyde salicylhydrazone and native cashew proteins immunotherapy, consequences in increased IgG_1 and IgG_{2a} anti- native cashew proteins ranges concerned with placebo.

The best examined treatment for the eradication of seed or any type of allergy at present time is by the evading of allergen. The best way to eradicate tree nuts, seeds or peanuts from the diet has no nutritional consequences for the majority of the individuals. Children suffering from food allergy are suggested to bring their own lunch box to school and advised not to share with other classmates. In common food preparation and eating areas, where majority of children are severely allergic to tree nut or peanut, foods containing nuts are strictly avoided. In preschool or childcare centers, there is maximum chance of food contamination for children of different age groups because of having same toys or eating areas. The center

management entreats that parents are not allowed to deliver foods having nuts in the lunch box to lower the chance of nut allergy. The digestion of pepsin in case of allergens exhibits to lower the allergencity, particular in the reference of oral allergy syndrome (Schimek et al., 2005) but also for food allergens (Untersmayr et al., 2007). The individuals in whom high-related quality of life (HRQL) is more significant may gain medical attention due to their food allergies than food allergic individuals.

4. Effect of Processing on Cashew Nuts

The processing of cashew nuts in shell is difficult and expensive due to the specific characteristics of the shell. The effect of various processing techniques on cashew nut allergens had been studied by Venkatachalam et al. (2008), they studied three well known allergens. γ-irradiation, roasting, pH variations, blanching, microwave treatments and autoclaving were different processing techniques. The roasting process resulted in significant decrease in the reactivity of Ana o 3 and Ana o 1 allergens and when high temperature about 200 °C was given for 15 minutes, due to increase in the strength of secondary structure of protein, the reactivity of Ana o 2 was also increased. The stability power of peanut allergens increase after the processing, which indicates that peanut allergens Ara h 3, Ara h 1 and Ara h 2/Ara h 6 are present in minor quantity. After the processing, the stability power of allergens increased and it's difficult to explain the exact origin of raised stability, researchers has performed many tries and struggle to understand the structural confirmation by the use of molecular dynamics simulations (Koppelman et al., 2005a; Koppelman, Hefle, Taylor & Jong, 2010; Vanga, Singh & Raghavan, 2015c). Similar research studies can be done on Ana o 2 allergens for additional investigating marvel of enlarged constancy afterward the thermal processing of allergen.

Moreover, various thermal treatments such as autoclaving, blanching, frying and microwave heating were applied to reduce the immune-reactivity of cashew nut and it was found that these treatments had no effect on cashew nut allergens. Meanwhile the treatments of γ-irradiation also exhibited no substantial alteration in the evaluation of protein reactivity that all the allergens are maximum heat stable (Venkatachalam et al., 2008). Similarly, in the study of Su et al. (2004), it was found that the effectiveness of γ-irradiation revealed no significant change or reduction in the reactivity of allergens. Although, the clinical consequence is uncertain as complete decline in immune reactivity with human serum has not been investigated (Mattison, Grimm & Wasserman**,** 2014).

5. Clinical Features

Allergies to cashew are increasing in prevalence, with clinical symptoms ranging from oral pruritus to fatal anaphylactic reaction (Archila et al., 2016). Few clinical studies are published on the topic of cashew nut allergy. Almost five pertinent researches are performed to inspect clinical indicators (Valk et al., 2014). Individuals facing allergy due to cashew mostly exhibit skin diseases monitored by respiratory and gastro-intestinal indications. Recent research revealed that minimum quantity of cashew nut allergen is able the source of unembellished clinical response. This also reveals the great effectiveness of the nut in contrast to the other various tree nuts and peanuts (Davoren & Peake, 2005). According to this study about 74 percent cashew nut and 30 percent peanut trigger individuals having tree nut and peanut allergy. Allergic individuals should avoid from the intake of these allergen food, otherwise it may cause serious anaphylactic reaction. The most unfavorable allergic reaction which is caused by after the ingestion of cashew nut is skin lesion follow by respiratory and gastrointestinal symptoms.

There is a case study which is proposed by Clark, Anagnostou & Ewan (2007), in which they used those children who had severe allergic attack after peanuts and cashew nuts intake and resulted in positive skin prick test. Children whose bodies show serious allergic reaction after the intake of cashew nuts were coordinated with those children whose body show serious allergic reaction after the intake of peanuts and the ratio was 2:1. According to study there is no major difference in medical structures of both cashew nut and peanut group, excluding asthma which is seems to be more common in peanut group. This study reported that allergic reactions to cashew nuts are often more severe than reactions to peanuts, with more frequent bronchoconstriction and cardiovascular symptoms in the cashew group despite the fact that asthma was a more frequent co-morbidity in the peanut group.

In Melbourne at Royal Children's Hospital; approximately 117 anaphylaxis reactions occur in 5 year period and in these cases, cashew nut allergens reactivity is more obvious than peanut allergens reactivity (18% and 13%, respectively). These percentages may not consider for other risk factors, because it is not declared whether these variations are statistically important or not (Silva et al., 2008). Davoren & Peake (2005) exposed in his study, 5 out of 27 patients who had cashew nut allergy, show serious allergic reactions just because of skin or mucosal contact. 5 out of 27 patients practiced anaphylaxis just because of mucosal or skin contact. It was found that anaphylaxis reactions were more even at less cashew nut allergy. Medical history of an individual in combination with the consequences of either skin prick test (SPT) or specific IgE (sIgE) test. Both these test are sometimes utilized to develop the identification of cashew nut allergy. Double-blind placebo-controlled food

challenge (DBPCFC) test is said to be the standard test for testing the cashew nut allergy in many individuals. The examination of various other foods, the latter one test is not able for the identification in a better way between clinical allergy and asymptomatic sensitization.

The symptoms in reference to medical are alienated into two types such as anaphylaxis and non-anaphylaxis. Anaphylaxis is said to be the increasing progressed multisystem allergic reaction in general that is use to characterize one or more than one signs or identification of respiratory and also cardiovascular diseases and skin or gastrointestinal tract diseases (Anaphylaxis Working Party of the Australasian Society of Clinical Immunology, Allergy (ASCIA). Non-anaphylaxis symptoms are said to be related to skin diseases as well as gastrointestinal indications not having respiratory or cardiovascular symptoms. Individuals face various reactions before seeing the negative clinical effects. The reactions are said to be influential if intake of food or relation with the alleged nut exhibits consequences in a reaction during 60 minutes of revelation.

In recent research it was found potent for observing the medical immunotherapy for the allergy that is caused by food in which both structural and linear epitopes are studied (Albrecht et al., 2009; Ditto et al., 2010). It was also observed that nonoral courses of sensitization including the epicutaneous courses do must occur (Strid et al., 2005). It was commonly observed that anaphylaxis is very much communal in the cashew collection. This strategy satisfies the medicinal wariness and the various discoveries. Cashew is found not to be much significant allergen in case of peanut; however, cashew allergy is concerned with a maximum chance of anaphylaxis (Hourihane et al., 2001).

Place Table 1 here

Infant's intake the appropriate amounts of nut. They exhibit the substantial amount that is able to progress the indication of anaphylaxis. In number of individuals the symptoms on skin and oral mucosal contact is found in reference to anaphylaxis. If nut allergens transfer from hand to mouth, it may cause serious reaction even from minute quantity. In different individuals, the symptoms appearing on skin could be the most mutual and collective in respect to non-anaphylactic indications categorized, keeping in view all the observations and hypothesis by different researchers (Sicherer, Burks & Sampson, 1998; Ewan, 1996). Many enduring individuals exhibits the indications related to anaphylaxis without exhibiting the indications on skin, this observation is also observed by others (Rance, Bidat, Bourrier & Sabouraud, 2003). It has become a potent medical allegation because some medical consultant did not diagnose anaphylaxis in the absence of skin indications.

Although a qualified food and drug administration health claim exists for nut and heart health, cashew have been exempt from its use because cashews exceed the disqualifying amount of saturated fatty acids. Approximately one-third of the saturated fat in cashews is stearic acid, which is relatively neutral on blood lipids, thereby suggesting that cashews could have effects that are similar to those of other nuts. However, clinical data on cashews and blood lipids have been limited (Mah et al., 2017). In a study, Mohan et al. (2018) reported that besides negative effects, cashew nut consumption is associated with increasing the levels of high density lipoprotein in serum and decreasing the levels of low density lipoprotein, cholesterol and triglyceride in blood. This positive effect is associated with the mitigation of risk factors of diabetes especially type II diabetes. The same effect of cashew nut intake against cholesterol parameters has been observed by Mah et al. (2017).

Additionally, antioxidant effects of anacardic acids present in cashew nuts have an area of interest in recent research with findings suggesting potential therapeutic use for certain diseases. These are associated with the prevention of behavioral changes and oxidative stress induced by rotenone in a rat model of Parkinson's disease or these compounds have promising neuroprotective action against degenerative changes in Parkinson's disease (Medeiros-Linard et al., 2018). According to Davis et al. (2007), adding cashew nuts in the diet resulted in an increased antioxidant capacity in subjects with metabolic syndrome. Moreover, the benefits of the addition of nuts in a healthy diet in front of a low fat diet have been recently highlighted by Estruch et al. (2013) confirming that the incidence of major cardiovascular events and mortality is 30 % lower for those individuals consuming a Mediterranean diet supplemented with a handful of nuts a day, compared to those that are advised to consume a low fat diet.

6. Diagnosis

Diagnosis of cashew nut allergy includes some parameters like history, in combination with *in vitro* specific IgE tests and measuring sensitization by skin prick test. Different researches on diagnosis of cashew nut allergy reported that majority of the children had consumed the specific relevant nut and many of these children experienced anaphylactic symptoms. These groups exhibited such symptoms, which were just like non-anaphylactic symptoms that is exactly match with the findings of previous authors (Ewan, 1996). Most of patients had anaphylaxis without the involvement of cutaneous (Hourihane et al., 2001). The individuals having positive or negative cashew nut experimental observations are not able to set apart in intermediate cashew nut mediated by sIgE. Skin prick tests are examined to have high rates in reference to sIgE for investigating the consequences of the challenge (Corderoy,

Sullivan & Nolan, 2011). Various factors are involved in the reliability of skin prick test that includes agar, method of the skin prick tests and quality of the extracted material.

A supposed illustration related to allergy was determined which in future can take the place of double-blind placebo-controlled food challenge test. It was authorized in the center that the representative exhibits an AUC of 0.97 to investigate allergy (Galvin et al., 2010). This representative model is however not capable to investigate allergy in a Dutch study (Klemans et al., 2013). A representative model is not yet been able to investigate the symptoms of cashew nut allergy. Still there is no investigation reported in reference to the importance of sensitization in combination to most of allergens of cashew to investigate medical reactions in reference to cashew nut or the mildness of those reactions (Valk et al., 2016).

Place Table 2 here

7. Management

Feed and food enzymes is a million-dollar industry worldwide (Fernandes, 2010; Gavrilescu, 2005). Many researches confirmed the significant effects on lowering the reactivity of allergens through enzymatic processing of cashew nuts by preventing the IgE binding to nut allergens. For instance, after following treatment with proteases, IgE binding to allergens from peanut flour and whole roasted peanuts has been efficiently reduced (Shi et al., 2013; Li, Yu, Ahmedna & Goktepe, 2013). Likewise, upon treating cashew proteins with pepsin showed reduction in IgE binding and this was confirmed by studying cashew allergy immunotherapy using a mouse model (Li et al., 2003). The *Aspergillus* genus is gaining much wideness and importance in the food processing industry. They are said to be *m*etabolically miscellaneous and causes variations in the gene expression in result of amendment in the conditions of the culture media (Duran et al., 2014). Moreover, Aspergilli are considered as important fungi for enzyme identification and nut allergens degradation to prevent allergic reactions from protein and these are produced on large scale. Generally, natural contaminants present in cashew nut are A. niger and oryzae (Midorikawa et al., 2008).

The prevalence of cashew nut allergy seems to be rising in industrialised countries with the increasing consumption of this nut. But there is still no cure for cashew nut allergy, as well as for other food allergies; thus, the allergic patients are advised to eliminate it from their diets. Nowadays, the trend of oral immunotherapy is in pipeline for the treatment of allergies. Oral immunotherapy for food including milk, egg and peanut are said to be the important technique to convince tolerance or desensitization, such as the doses schedule and side-effects. Additionally, restriction of plant based foods and at the same time consumption

of related foods as a substitute such as epistachio as a replacer for cashew nut. Further research is necessary for the betterment underpin a suggestion on circumvent of botanically relevant foods with allergenic homology to cashew nut. In a study, Weinberger and Sicherer (2018) reported the management for cashew nut allergy. They found that patients with tree nuts allergies should avoid the consumption of causal nut(s) and there should be prompt treatment of symptoms upon accidental exposure. A specific consideration with regard to the management of tree nut allergy is the decision to avoid all tree nuts or only the tree nuts to which a patient is clinically allergic. There are currently no data on the primary or secondary prevention of tree nuts allergy. Treatment strategies are being evaluated.

The most common food that have severe anaphylactic causing reactions (although some reactions to nuts are not severe) are the nut allergy and because of it most of the cases doctors always suggests adrenaline pens for nut allergies the reason is that there is no test that can forecast about the risk of anaphylaxis. A very safe and effective hormone against food allergy is Adrenaline because they are excessively used as crucial step in management. Accordingly, when carefully choosing processed foods that are commercially available, the allergic consumers have to rely on proper food labelling. In this sense, the control of labelling compliance is much needed, which has prompted the development of proficient analytical methods for allergen analysis (Mendes et al., 2016).

Many people have serious allergic reaction after the ingestion of specific tree nut, these kinds of people are able to bear other tree nuts, but mostly allergists advice these patients to avoid use of other tree nuts to prevent anaphylactic reaction. There are many uses of tree nuts, frequently used for the garnishing of salads, for ice cream topping, in baked goods and as an ingredient in Asian dishes. The eight most common food allergens are tree nuts, affecting children and adults, if tree nuts are added in any food item, are specifically mentioned in the food labels and Consumer Protection Act (FALCPA) of 2004. If tree nuts are used in the manufacturing of food products, it must be mentioned on food labels to facilitate the people.

Some companies may include the information's that their food products don't contain. This kind of statement is not required by law. Therefore, it is necessary for people with tree nut allergy to read the food labels carefully. In the distillation process, nuts and nut flavors may be added in some carbonated beverages. Most alcoholic beverages are not fulfilled by the food labels and Consumer Protection Act requirements; if "botanicals" or "natural flavors" are highlighted on ingredient list, it is necessary for you to call manufacturer to verify whether the ingredient list indicates the presence of flavoring nut or nuts. Tree nut oils,

which may include nut protein, can be found in hair care products, soaps and lotions. People those have allergy with tree nuts should avoid from the use of these products.

Moreover, cashews are used in cooking in the Far East and in the Indian sub-continent and may be found in ethnic food from those areas. Therefore, people with severe nut allergy should avoid Asian restaurants such as Indian, Chinese, Thai, because nuts are so commonly used as ingredients, and there is also a risk of cross-contamination. Additionally, cashews can be used in baking especially in Eastern pastries and in confectionery items, sweets, ice creams and chocolates and now a days, cashew nut butter is available in supermarkets as well as whole food shops, so these products should be avoided by allergy patients.

8. Conclusion

Normally, cashew nut allergy is concerned with the disease called anaphylaxis. There is a dire need to give same importance as peanut allergy, and extensive awareness to the general public and medical practitioners about its sternness is necessary. Anaphylaxis tree nuts and peanuts can exhibit without involvement of cutaneous. Respiratory symptoms are the most common anaphylactic symptom in the children. According to clinical investigation, about children are more sensitized against cashew nut so far. Cashew nuts may lead to severe allergic reactions such as anaphylaxis. The chief allergenic proteins present in cashew nuts are 2S albumins and legume-like proteins. Recently, standard tool to detect this allergy is double-blind placebo-controlled food challenge test. This test is however costly and time taken for sufferers of the disease. In case of a cashew nut allergy, restricting the use of pistachio nuts must be recommended, but suggestion of avoidance of other related allergens requires furthermore investigation. Conclusively, cashew nut may be reflected as a remarkably potent allergen, frequently causing anaphylaxis and other treacherous sort of aversion.

Conflict of interest

All the authors declare no conflict of interests.

Authors Contribution

All the authors have equally contributed in preparation of this paper.

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Table 1. Clinical symptoms reported for cashew nuts.

Allergic reactions	Symptoms	Number of cases
Anaphylaxis	Respiratory/skin/GIT	5 (25)
	Respiratory	3 (15)
	Respiratory and skin	8 (40)
	Respiratory and GIT	3 (15)
	CVS/skin/GIT	0
	Respiratory/CVS/skin	1 (5)
Non-anaphylaxis	Skin/GIT	0
	GIT	0
	Skin	7 (100)

GIT, gastrointestinal tract; CVS, cardiovascular system.

Table 2. Relevant studies on clinical symptoms of cashew nut allergy

No.	Type of study	Number of cases	Children/adults	Symptoms (% and n= number of cases)	References
1	Retrospective study	29	Children and adults	Wheeze: 48% (14/29) Collapse/feeling faint: 38% (11/29)	Hourihane et al. (2000)
2	Prospective study	42	Children	Respiratory 25% (28/112) Cutaneous 56% (63/112) Gastro-intestinal 17% (19/112)	Rance et al. (2003)
3	Case-matching study	47	Children	Cutaneous: 98% (46/47) Gastro-intestinal: 32% (15/47) Rhino-conjunctivitis: 6% (3/47) Wheeze: 40% (19/47) Laryngeal oedema: 9% (4/47) Cardiovascular: 13% (6/47) Lightheaded: 13% (6/47)	Clark et al. (2007)
4	Retrospective chart review	16	Children	Anaphylaxis: 50% (8/16) Respiratory: 50% (8/16) Cutaneous: 72.4% (11/16) Gastro-intestinal: 18.8% (3/16) Eye symptoms: 18.8% (3/16)	Grigg et al. (2009)

5	Retrospective chart review	27	Children	Anaphylaxis: 74.1% (20/27) Respiratory: 15% (3/20) Respiratory, cardiovascular system, skin: 5% (1/20) Respiratory, skin, gastro-intestinal 25% (5/20) Respiratory and skin: 40% (8/20) Respiratory and gastro-intestinal 15% (3/20) Nonanaphylaxis: 25.9% (7/27) Skin 100% (7/7)	Davoren et al. (2011)
6	Retrospective chart review	100	Children	With history of cashew nut allergy	York et al. (2011)
7	Retrospective chart review	-	Children	Low specific IgE	Corderoy et al. (2011)
8	Retrospective chart review	27	Adults	Anaphylaxis (74%)	Davoren and Peake (2005)
9	Case-matching study	-	Adults	Wheezing Cardiovascular symptoms	Clark et al. (2007)

Highlights

1. Encouraging awareness in public for cashew nut allergy
2. Highlighting prevalence of cashew nut allergy
3. Evaluating epidemiology of cashew nut allergy
4. Revealing diagnosis methods and management of cashew nut allergy