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FACULDADE DE CIÊNCIAS DA NUTRIÇÃO E ALIMENTAÇÃO
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Asthma and Mediterranean Diet

Asma e Alimentação Mediterrânica

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Abstract

Asthma is one of the most common chronic disease in childhood, imposing a huge burden on the patient, their family and society. There is evidence that its prevalence has increased over the last decades and is still increasing, despite there being some indications that the increase in prevalence may have plateaued in some countries in the last few years. It has been hypothesized that this increase is a consequence of changes in environmental and/or behavioral factors, namely the modification in dietary habits. A recent number of investigations agree that adherence to a Mediterranean dietary pattern can be associated with a decreased risk of current asthma symptoms. Although this evidence is promising, further research is needed.

Key words: Asthma, Mediterranean diet, dietary patterns, prevalence

Resumo

A Asma é uma das doenças crónicas mais comuns na infância, acarretando consigo um enorme ónus tanto para o paciente, como para a sua família e sociedade. Há estudos que mostram que a prevalência desta patologia tem vindo a aumentar nas últimas décadas, apesar de haver algumas indicações no sentido desta estar a estabilizar em alguns países. Algumas hipóteses sugerem que este aumento é consequência de mudanças ambientais e comportamentais, nomeadamente na modificação dos hábitos alimentares. Investigações recentes assumem que a adesão ao padrão mediterrânico pode estar associada a uma diminuição dos sintomas da asma. Embora esta conclusão seja promissora, é necessária uma investigação mais aprofundada.

Palavras-Chave: Asma, Dieta Mediterrânica, Padrões Alimentares, Prevalência

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1. Introduction

Asthma is a multifactorial and ordinary chronic inflammatory disorder of the airways, with a high prevalence in all age groups, but mostly in children and young adults, and it is a serious public health problem in several countries throughout the world[1-3].

This review considers the current scientific evidence for the association between Mediterranean dietary and asthma.

2. Asthma

Although there is no standard asthma definition, a description has been proposed by the Global Initiative for Asthma (GINA) based on the functional consequences of the airways inflammation: Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable airflow obstruction within the lung and is often reversible either spontaneously or with treatment[4].

2.1. The Prevalence of Asthma

The prevalence of asthma has markedly increased in the last decades, especially in children in the western world, originating what has been referred to as an

‘‘allergy epidemic”[5-9]. Nowadays, it is estimated that this disease affects approximately 300 million people and that is causes 250 thousand annual deaths [4, 10]. It is estimated that by 2025 there could be an additional 100 million people affected by this disease[1, 11]. The areas of the world's highest prevalence of asthma are in North America, Latin America and Australia (Figure 1).

Nevertheless, recent evidence from epidemiological studies suggests that the prevalence of asthma reached a plateau in most industrialized countries, and may now be declining due to earlier detection and improved treatment[3, 12-14]. In Europe, the prevalence of this disease ranges from 18.4% (Scotland) to 1.3% (Albania) (Table1).

In particular, studies indicate that the prevalence of asthma in Portugal is 11.0% in children (6-7 years), 11.8% in adolescents (13-14 years) and 5.2% in adults (20-44 years)[15, 16].

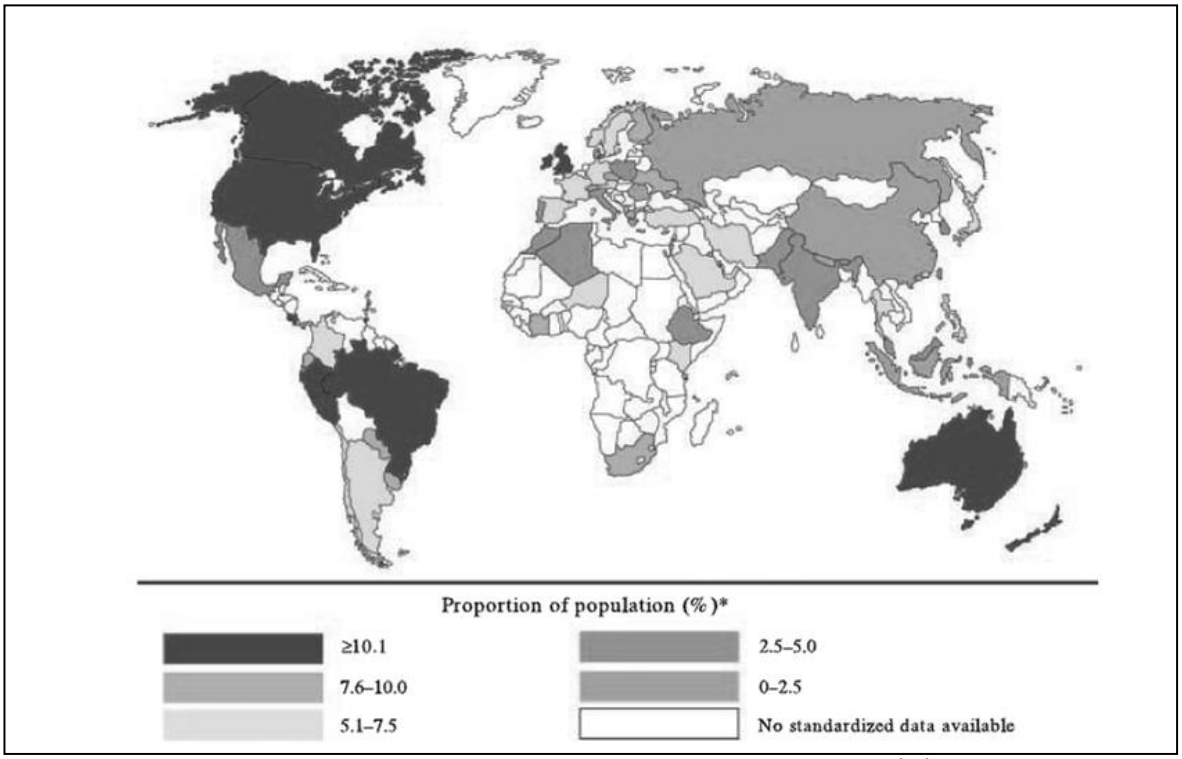

Figure 1 - Worldwide prevalence of clinical asthma[11]

Table 1 - Prevalence of Clinical Asthma in Europe (adapted from Masoli et al.)[11]

Country	Prevalence %
Scotland	18.4
Wales	16.8
England	15.3
Republic of Ireland	14.6
Malta	8.0
Belgium	6.0
Austria	5.8
Spain	5.7
Estonia	5.4
Portugal	4.8
Italy	4.5
Poland	4.1
Denmark	3.0
Greece	1.9
Albania	1.3

2.2. Social and Economic Burden

Asthma represents a serious economic and social impact in health care systems, on patients' quality of life and on society as a whole[4, 12, 17, 18].

In the economic analysis of asthma both direct medical costs as well as indirect non-medical costs need to be accounted for[4]. On the one hand, hospital admissions and medications entail high costs for people and for health care systems[19]. On the other hand, this disease is one of the most common causes of

school and work absenteeism[20, 21]. Moreover, asthma is a major cause of disability and/or restricted activity among children, namely playing a musical instrument and participating in more intense physical activities; it may even affect sleep patterns and hence have a negative impact in academic and career success due to poor attendance as well as lower productivity associated with asthma attacks[17, 22].

2.3. Factors influencing the Development and Expression of Asthma

It is believed that over 70% of the variation in asthmatic tendency is explained by genetic factors[6]. However, the high variation in asthma prevalence among countries and/or geographically adjacent areas, over a considerably short period of time, suggests that environmental factors may play a determinant role in asthma prevalence and severity[9, 23, 24].

Thereby, asthma is considered to be a rather complex interaction between genes and environment[6].

The factors that can influence the risk of asthma can be divided in two groups: the host factors and the environmental factors (Table 2)[4].

Amongst the environmental factors, several dietary hypotheses have been proposed and, somewhat surprisingly, changing diet has emerged as a promising candidate to the increase of asthma[1]. Indeed, the evolution from a more traditional dietary pattern to a modern westernised one and its effects on asthma led to the discussion of several hypotheses: the increase in asthma related to a) declining dietary antioxidant intake; b) decreased intake of long-chain n-3

polyunsaturated fatty acids (PUFA) and increasing intake of n-6 PUFA; c) Vitamin D supplementation or in the opposite deficiency; among many other possibilities

Table 2 - Factors influencing the development and expression of Asthm[4-6]

Host Factors	Environmental Factors
	Allergens
Genetic	Infections
Obesity	Occupational Sensitizers
Sex	Tobacco Smoke
	Outdoor/Indoor air pollution
	Climate
	Diet
	Socioeconomic level
	Lifestyle
	Population hygiene

2.3.1. Antioxidant Hypothesis

In 1994, it was suggested that alteration in diet associated to the declining in dietary intakes of antioxidant-rich foods, i.e. foods containing vitamins A, C, E, and oligoelements such as zinc and selenium, and others, could be responsible for the increase in asthma prevalence[1, 6]. The mechanism proposed in the original antioxidant hypothesis relates declining lung antioxidant defences to increased oxidant-induced airway damage, airway inflammation and asthma. However,

current research suggests that this oxidant–antioxidant model is most likely a minor mechanism and that biological effects which are independent of antioxidant properties may be more plausible[26].

2.3.2. Lipid Hypothesis

In 1997, changes in dietary fat intake in Westernized countries were suggested to contribute to the increase in asthma[26]. The dietary intake of saturated fats (mainly from butter and lard) decreased and the intake of n-6 PUFA (from margarine and vegetable oils) increased, most likely as a response to public health measures to reduce heart diseases. However, on the one hand foods high in saturated fatty acids, such as butter, whole milk and non-pasteurised farm milk, have been consistently associated with a reduced risk of asthma. On the other hand, it has been suggested that higher margarine intake rich in n-6 PUFA is associated with an increased risk of asthma and hay fever in adulthood, and eczema and allergic sensitization in children[27]. Moreover, the increasing intake of n-6 PUFA and decreasing intake of n-3 PUFA, predominantly from fresh oily fish and derived fish oil products, has contributed to the increase in allergic disease and consequently asthma[1]. Overall, the body of observational evidence relating PUFA to asthma is weak.

2.3.3. Vitamin D Hypothesis

Two contradictory hypotheses relate vitamin D to asthma and allergy[1]. In 2007, Litonjua and Weiss hypothesised that vitamin D deficiency could increase asthma prevalence in young children[28]. Currently, the inability to compensate this vitamin

directly through the diet as well as the increasing predisposition to stay indoors, avoiding the sunshine as skin cancer prevention, are the most likely reasons for the insufficient intake of vitamin D[1, 26, 28].

In contrast, in 1999 it was postulated that the increase in asthma and allergy was a result of widespread rickets prophylaxis with vitamin D supplements in Westernised countries, emphasizing the effects of vitamin D in promoting Th-cell differentiation towards the Th2 phenotype[1, 26].

3. Dietary Patterns *versus* Single Nutrients

The majority of studies in nutritional epidemiology analyse the development of diseases in relation to specific nutrients or foods[29]. Although this type of analysis has been quite valuable, it has several conceptual and methodological limitations. First of all, people consume meals with a variety of products, combining different nutrients which are likely to be interactive or synergistic amongst them; not isolated nutrients[30]. Secondly, the high correlation among some nutrients unable a thorough examination of their separate effects, when they are entered into a model simultaneously[7]. Thirdly, the effect of a single nutrient may be too small to be significant; nonetheless, the jointed effects of numerous nutrients included in a dietary pattern may be too large to be detectable[31].

Recently, the analysis of dietary patterns has emerged with a different, yet complementary approach to analyse the correlation between the diet and the emergence of chronic diseases. Instead of considering individual nutrients or foods, pattern analysis examines the effects of diet in general[31].

4. Mediterranean Diet

It has been hypothesized that the rise in the occurrence of asthma in western societies could be related to changed dietary habits since the 1950s[32] – specifically, the introduction of fast food in the western diet, with decreased consumption of fresh fruit, vegetables, fish and milk[7, 33, 34]. This is in contrast to the traditional diet, which comprised fresh food that was produced and marketed locally and was eaten shortly after harvesting[35].

The Mediterranean Diet (MD), a cultural model of healthy eating, has been object of study since the 1950s, when its characteristics were first defined and put together into a dietary pattern. Nowadays, its benefits for health are well recognized[36]. In fact, it has been associated with lower incidence of mortality and morbidity by chronic diseases[23, 30, 37-42].

The traditional Mediterranean diet is characterized by a high intake of fruits and vegetables, whole grain cereals, pulses and nuts. Olive oil (a monounsaturated fatty acid) serves as the principal source of fat. It is moderate in dairy products, mostly cheese and yogurt, low intake frequency of red meat and it is modest in wine consumption[23, 29, 37, 40, 43, 44].

The Mediterranean diet pattern has a graphic representation: The Mediterranean Diet Pyramid (Figure 2).

The current pattern of the Mediterranean Pyramid provides not only quantitative key tips for choosing food but also qualitative ones. It indicates the relative proportions and frequencies of consumption of the major food groups which are part of the regular Mediterranean pattern[45].

Moreover, it provides figurative information about healthy lifestyles and cultural elements that should also be considered in order to acquire all the benefits from the Mediterranean diet.

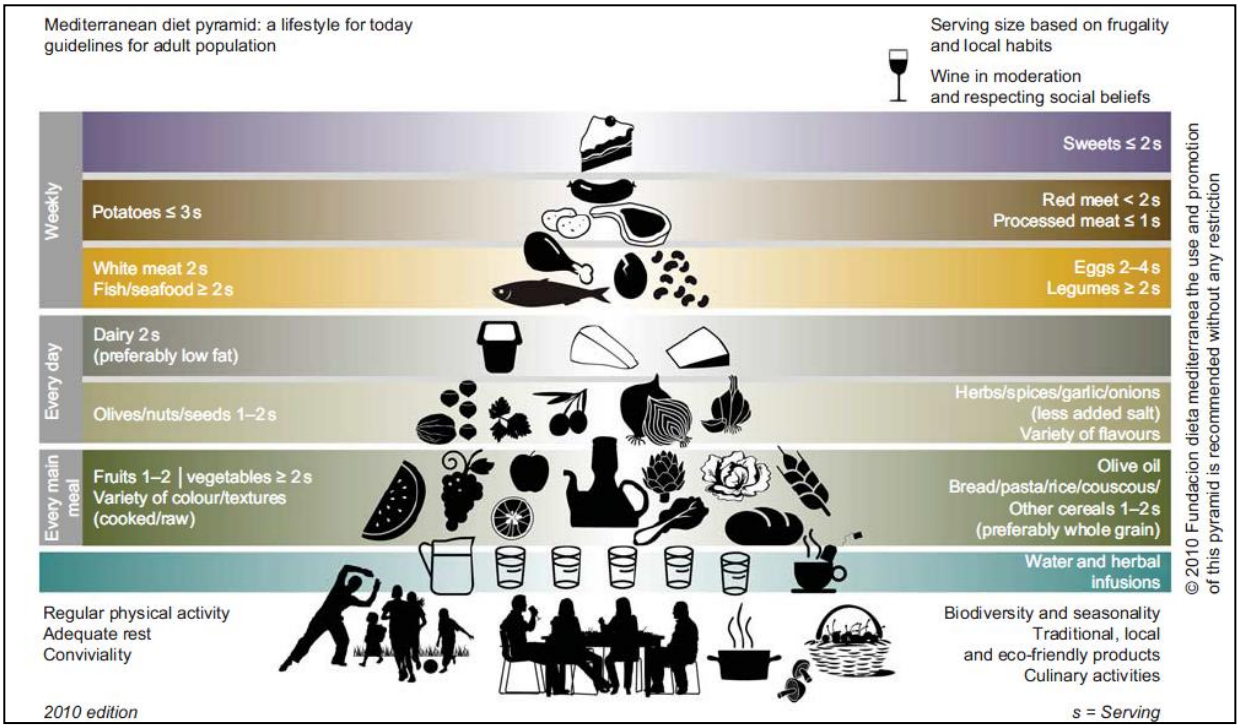

Figure 2 – Mediterranean Diet Pyramid[45]

5. Mediterranean Diet and Asthma

Recent studies address the thesis that Mediterranean diet may be protective against the development of asthma as well as improve the impact of its symptoms[29, 46]. Some studies relating Mediterranean diet and asthma are summarized in Table 3.

Barros et al., reports that high adherence to Mediterranean Diet and its typical components, such as fresh fruits and nuts, may increase the likelihood of asthma

Table 3 - Summary of studies and their findings regarding dietary factors and lung function				
Author	**Design**	**Sample**	**Country**	**Main Findings**
De Batle et al.[13]	Cross-sectional	1476 Children, 6-7 years	Mexicali region, Mexico	Mediterranean Diet (MD) offers a protective effect against asthma and allergic rhinitis
Barros R., et al.[23]	Cross-sectional	174 Adults	Portugal	High adherence to traditional MD increased likelihood of asthma control
Chatzi et al.[47]	Cross-sectional	690 Children, 7-18 years	Crete, Greece	Consumption of fruits, vegetables, nuts and a high adherence to a traditional MD have beneficial effects on asthma and rhinitis
Gonzalez et al.[48]	Cross-sectional	14700 Children and Adolescents	Galicia, Spain	Greater adherence to MD is associated with higher risk of severe asthma
Garcia-Marcos et al.[49]	Cross-sectional	20106 Children, 6-7 years	Spain	A Mediterranean diet has a potentially protective effect in girls aged 6-7 years
Arvantini et al.[29]	Cross-sectional	700 Children, 10-12 years	Athens, Greece	Inverse relationship between level of adherence to Mediterranean diet and prevalence of asthma
Chatzi et al.[50]	Review of the literature	-	-	High level of adherence to the Mediterranean diet early in life protects against the development of asthma and atopy in children
Castro-Rodriguez[43]	Cross-sectional	1784 Children, 4 years	Murcia, Spain	The MD is an independent protective factor for current wheezing in pre-schoolers, irrespective of obesity and physical activity
Tabak et al.[32]	Cross-sectional	598 Children, 8-13 years	The Netherlands	High intake of whole grain products and fish may have a protective effect against asthma in children. No clear association of citrus fruit, vegetables, and dairy products intake and asthma
Cook et al.[51]	Cross-sectional	2650 children, 8 -11 years	England	Fresh fruit consumption appears to have a beneficial effect on lung function in children.
Ellwood et al.[35]	Cross-sectional	721 601 Children	56 different countries	Negative association between vegetable consumption and asthma
Farchi et al.[33]	Cross-sectional	5257 Children, 6-7 years	Italy	High consumption of fruits and vegetables may reduce wheezing symptoms

control in adults[23]. In rural areas of Crete, a protective effect of fruits, vegetables and nuts on self-reported wheezing in children and adolescents was observed[47]. Another study in Mexican children showed that a greater adherence to a Mediterranean dietary patterns was associated with having less asthma, wheezing allergic rhinitis and current sneezing[13]. In a Spanish multicentre study, Mediterranean Diet decreased the risk of severe asthma in school aged girls[49]. Arvantini et al. shows that there is an inverse relationship between the level of adherence to Mediterranean diet and prevalence of asthma in school-aged children[29]. Mediterranean diet has key elements that have been suggested to be responsible for the beneficial effect of diet on human health in general and potentially protective for asthma in particular.

With regards to the Mediterranean diet during pregnancy and its impact on asthma, there are some recent studies suggesting that a high level of adherence to the Mediterranean diet in maternal and early life play a role in the child's immune system development and protects against the development of asthma and atopy in children[50, 52]. More specifically, consumption of vegetables more than eight times per week was inversely associated with persistent wheeze and atopy. Fish intake more than two to three times per week and legumes intake more than once per week were inversely associated with persistent wheeze. In contrast, an increased intake of red meat (more than three to four times per week) showed a trend towards positive associations with persistent wheeze and atopic wheeze in offspring [50, 52]. It was also reported that olive oil (component of the Mediterranean diet), used as the main source of oil for cooking or dressing salads during pregnancy, is associated with less wheezing of the children during their first year of life[53]. The main active components of olive oil include oleic acid, phenolic

derivatives (hydroxytyrosol, tyrosol, oleuropein, and ligstroside) and squelene, all of which have been found to exhibit a marked antioxidant activity; oleuropein and its hydrolysis product (hydroxytyrosol) being the most potent antioxidants[53].

Several studies reported that a greater intake of fresh fruit and vegetables is related to a lower prevalence of respiratory symptoms[23, 51, 54, 55]. In fact, these foods may provide fibre and antioxidants, which may reduce endogenous oxidative stress related to inflammatory diseases[13, 23]. Furthermore, fruits and vegetables are extremely rich in vitamins C, E, ß-carotene, magnesium, and selenium which are associated with reduction in asthma prevalence and may prevent or limit an inflammatory response in the airways by reducing reactive oxygen species and inhibiting lipid peroxidation[29, 47, 56]. In addition, flavonoids, antioxidants frequently found in fruits and red wine, may have anti-allergic and anti-inflammatory effects[28]. These are associated with reduction in asthma prevalence and may prevent or limit an inflammatory response in the airways by reducing reactive oxygen species and inhibiting lipid peroxidation[29, 47].

On the other hand, the Mediterranean diet encourages the consumption of nuts, including almonds, hazelnuts, walnuts, peanuts, pine nuts, pistachios and cashews, which contain a high proportion of monounsaturated (MUFA) and α-linolenic acid, fibres, vitamins (folate, vitamins E and B6), minerals (copper, magnesium, zinc and selenium) and many bioactive compounds, including a variety of polyphenols that may modulate redox status, inflammatory and immune response[23].

Additionally, the relatively high consumption of fatty fish (e.g. sardine, tuna, salmon), source of n-3 fatty acids, combined with low n-6 consumption from dietary fats is typical in a Mediterranean diet. This high n-3/ n-6 fatty acid ratio

reduces the levels of pro-inflammatory cytokines (that are increased in asthmatic subjects) and influences the differentiation of T-helper lymphocytes[13, 54]. Furthermore, long-chain n-3 PUFA decreases the production of inflammatory mediators, competitively inhibiting the metabolism of arachidonic acid (generating less active prostenoids and leukotrienes), suppressing IgE production, and thereby potentially acting to reduce airway inflammation and bronchoconstriction in asthma[27].

Cereals (particularly wholegrain) are rich in vitamin D, phenolic acids, and phytic acid which are antioxidants and anti-inflammatory helping in the treatment of asthma [29, 53].

Respecting religious and social beliefs, a moderate consumption of wine and other fermented beverages during meals (one glass per day for women and two glasses per day for men, as a generic reference) is recommended in this dietary pattern[45]. However, the Mediterranean Diet Score considers total ethanol intake, irrespective of the different alcoholic beverages[41]. On the opposite, ethanol intake was associated with increased risk of non-controlled asthma. Indeed, some studies show that alcohol consumption has been associated with hay fever symptoms, allergic sensitization and serum IgE[23, 57]. Hence, the association between specific beverages and asthma needs more investigation.

For all the stated reasons, high adherence to Mediterranean diet and to some of their typical components such as fresh fruits, vegetables, nuts, olive oil, and others, may have a protective role in asthma control.

6. Conclusions

Asthma is a multifactorial disease, and there is a general consistency in the evidence that a westernized diet seems to be associated with an increased risk of incidence and prevalence of this pathology.

Epidemiologic studies investigating the association between the intake of single nutrients and foods and asthma are very limited. However, dietary patterns, especially the Mediterranean, seem to have potential beneficial effects that should be taken into account. Therefore, health professionals should implement nutritional education as a means to improve healthy eating.

Because asthma and allergic diseases usually have their beginnings in early life, prospective birth studies are needed to investigate the role of diet during fetal and early life. Research on potential risk factors of asthma and respiratory allergies can enhance our understanding of geographic differences and support decisions on preventive strategies. In addition, multidisciplinary studies are required to investigate the complexity of dietary factors and understand the mechanisms of this protective effect, to evaluate the most relevant window of exposure, and to address specific components of diet in relation to asthma.

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