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A1 and A2 Milk: Myth vs. Reality- A mini review

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ABSTRACT

Milk has been considered a complete nutrition for all ages; there are many lobbies, who have been discouraging the use of milk citing health or cruelty reasons. More than 95% of cow milk is constituted by casein and whey proteins. Among the caseins, β-casein is the second most abundant milk protein and the different mutations in β-casein protein have led to 12 nucleotide variants and out of these A1 and A2 are the most common. The A2 variants of beta casein possess proline (CCT) at the 67th position of its 229 amino acid chain, while A1 variants with histidine (CAT) at the respective position due to a mutation. The A1 β-casein variants released β-casomorphin-7 (BCM-7) bioactive peptide by gastrointestinal proteolytic digestion. Several researchers have described that BCM-7 is associated as a risk factor for type-1 diabetes, coronary heart disease, arteriosclerosis, autism and schizophrenia. People, who consume milk containing high levels of β-casein A2 variant, have a lesser chance of cardiovascular disease and type-1 diabetes. While A2 milk is considered safe for human consumption and has a lower occurrence of cardiovascular disease and type-1 diabetes. Therefore, A1/A2 hypothesis is very interesting and important for public health concerns. This review article elaborates on the latest debate about the A1/A2 milk associated with impacts on public health.

1. Introduction

Milk is a complete meal for young ones and is considered to be one of the best foods from long back in history. The consumed milk is mostly from cattle, buffaloes, goats, sheep, and camels. Although any mammal can produce milk but the source of milk from dairy farms generally consists of high producing milch cow. Typically, the crossbred cow milk contains 12.62% total solids, 3.6% fat, 8.7% solid not fat, 5.31% lactose, 0.718% ash and 3.08 % protein, which are very essential for a growing kid, pregnant mother, a sick person or an old age people (Sharma *et al.*, 2018). Even though, considered a complete food, a new dimension to the debate was started in 1992, when the scientists in New Zealand reported a correlation between the type of milk consumed and the prevalence of type-1 diabetes, prostate and ovarian cancer. With an ongoing debate on the nutritional value of milk, a bunch of companies have laid out some research and concluded with the A1 and A2 types of milk. Currently, numerous companies have been advertising "A2 milk" as a healthier option than the "A1 milk". Here, we presented some of the findings of A1 and A2 milk and how they can produce adverse effects on our health.

2. What are A1 and A2 milk?

The major group of protein in milk is casein (3%) which is used for the production of cheese. The casein protein is further classified into alpha, beta, and gamma, in which beta-casein is the most prevalent casein protein. β-casein again comes in twelve genetic variants viz. A1, A2, A3, B, C, D, E, F, H1, H2, I, and G (Massella *et al.*, 2017). Among these, A1, A2 and B forms are the commonly found genetic variants (Farrell *et al.*, 2004). The only difference between A1 and A2

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β-casein protein is the single amino acid change at the "67th" position, where "Proline (CCT)" is present in A2 β-casein and "Histidine (CAT)" is found in A1 β-casein (Sodhi *et al.*, 2012). This single nucleotide polymorphism is mainly responsible for changes in digestion patterns. When consuming milk containing A1 β-casein, it releases a bioactive seven-amino-acid peptide known as "Beta-Casomorphin-7" (BCM-7) at the time of digestion in the small intestine, but BCM-7 was not present in A2 milk (Hartwig *et al.*, 1997). The BCM-7 peptide demonstrates a strong opioid activity, which stimulates human T lymphocyte proliferation in vitro (Kurek *et al.*, 1992, Gill *et al.*, 2000). It also has an inhibitory effect on immune function and is suspected to induce health risks like heart disease, type-I diabetes and sudden infant death syndrome (Jianqin *et al.*, 2016).

2.1 A1 milk history

A1 milk comes from Northern European native cow breeds such as Friesian, Ayrshire, British Shorthorn, and Holstein that contains A1 beta-casein. Since A1 milk contains BCM-7 opioids so it can potentially lead to adverse health problems such as hypertension, type-I diabetes, cardiovascular issues, intolerance of dairy products and even a slowing of cognitive processes (EFSA, 2009).

2.2 Why A1 milk is Devil?

Due to the presence of a BCM-7 in A1 milk, digestive enzymes acted in a different way than the A2 milk during the process of digestion (Figure 1). Beta-casomorphin-7 (BCM-7) is released by digestive enzymes from the A1 β -casein protein but the enzymes cannot split the A2 protein due to the presence of proline at that location (Noni, 2008). Hence, BCM-7 is not released from A2 β-casein protein digestion. Since, BCM-7 easily interacts with the human gastrointestinal tract and brainstem so that it is known as a "devil" in A1 milk (Truswell, 2005).

2.3 A2 milk history and their benefits

A2 milk comes from Southern French breeds of cow i.e., Channel Island cows, Guernsey, Jersey, Charolais and Limousin, and in the Zebu cattle of Africa and Asia, which does not release BCM-7 (Truswell *et al.,* 2005). Research from different countries provides different results, but the evidence proved that A1 milk carries potential health risks as compared to the consumption of A2 milk. Therefore, A2 milk Corporation was established in New Zealand by Dr. Corran McLachlan. For over many years ago, an Auckland-based company known as A2 Corporation has been exporting a brand of A2 milk in New Zealand and Australia and accounts for 8 % of Australia's dairy market.

In 2004, Australia's Queensland Health Department imposed a fine on A2 Corp for making false and misleading claims about the health benefits of its milk. A review by the European Food Safety Authority (EFSA) in 2009 found no link between the consumption of A1 milk, health, and digestive problems. In 2012, A2 Corp. introduced A2 milk in the United Kingdom through the Tesco chain, where a two-liter bottle sells about 18 percent more than conventional milk. The A1/A2 milk debate has raged for a long time in Australia, New Zealand, and Europe. Several researchers reported that the populations consuming more A2 milk than the A1 milk exhibited a lower incidence of cardiovascular disease, Type 1 diabetes (Sodhi *et al.,* 2012); less incidence of bloating and abdominal pain (Ho *et al.*, 2014).

3. The genetics behind A1 and A2 Milk

Around 5000 years back β-casein gene was mutated at 67th position (chromosome no. 6), amino acid was changed from proline (A2 allele) to histidine (A1 allele). Hence, the chances of three genotypes in cows i.e. A1A1 (homozygous) or A1A2 (heterozygous) or A2A2 (homozygous). The A1A2 cow produced both A1 and A2 type of allele. Whereas, A2A2 types of cow produce only the A2 allele and the A1A1 cow produce only the A1 allele. Therefore, A2A2 genotype cows transmit the A2 allele to progeny while A1A1 cows pass the A1 allele to their progeny but for heterozygous A1A2 cows, there is an equal chance of transmitting both the alleles.

Gene frequency of the A1 allele was reported to be very high (above 90%) in Holstein Friesian cows of North America and North Europe. In other hand, German Holstein Friesian (HF) contains a very high-frequency of A2 allele is

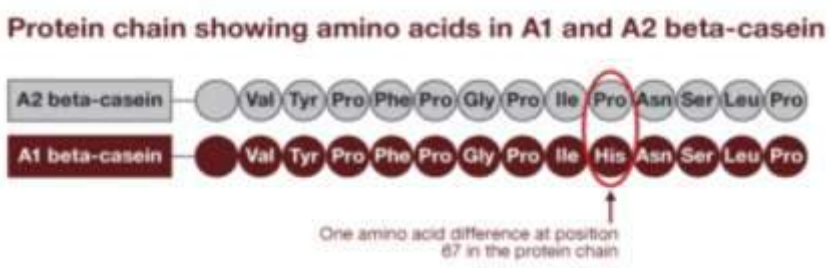

Figure 1. A2 and A1 beta casein differ only by amino acid at 67th position in 229 amino acid chain (source: www.drjockers.com)

Figure 2. A1 and A2 allele frequency in European cattle breeds (Parashar and Saini, 2015)

around 97 %. The Southern European breeds and the Jersey cattle breeds carry the A1 allele at about 35% and the A2 allele is 66.6 %. In the case of Guernsey cattle breeds carry the A1 allele less than 10% and the Scottish Ayrshire breed having more than 50% A1 allele (Parashar and Saini, 2015; Figure 2). Similarly, the frequency of the A1 allele in HF cattle is in the range of 40-65% while in the USA or European country, Guernsey cattle have a high A2 frequency (98 %) which is almost alike to our Indian breeds. Worldwide, A2 gene frequency is generally higher in Jersey cattle (60-80%) (Vet helpline India, 2015, www.downtoearth.org.in, snowvillecreamery.com). Therefore, based on various reports we can say that frequency of the A1 and A2 allele in the milch cattle breed is area-specific rather than breed-specific.

4. Status of A1/A2 milk variants in the Indian context

For a very long time, we venerated the cow as our mother and her milk as an elixir of life. As per Ayurveda, the five cow products (panch gavya) which contain cow milk possess miraculous healing properties. In recent times, due to controversy about milk being harmful to human health has caught the attention of the mass and it became a burning issue for many people. Urban people are aware of the debate between A1 and A2 types of milk, with A1 milk being harmful to human health and A2 milk is beneficial. But, the majority of people still don't know the facts behind the debate on the A1/A2 type of milk. Mishra *et al.,* 2009 reported that the indigenous cows, buffaloes produce only the A2 allele hence it is the source for the A2 type of milk only, whereas exotic cattle mostly produced A1 allele. Parashar and Saini (2015) reported that Indian milch breeds of cows (Red Sindhi, Sahiwal, Tharparkar, and Gir) and buffaloes carry 100% A2 allele, other desi milch breeds 94 percent and exotic cattle (HF and Jersey) produced approximately 60 percent of A2 allele (Figure 3). Ng-Kwai-Hang and Grosclaude (2002) reported A1 β-casein is absent in the milk of pure Asian and African cattle. Moreover, National Bureau of Animal Genetic Resources (NBAGR) also screened 615 cattle representing 15 Indian cattle breeds. Out of these, 13 breeds were reported to have A2A2 genotypes and two cattle breeds Malenadu Gidda and Kherigarh had A1A2 genotypes. Similarly, NBAGR (2012) screened 180 bulls at random from different regions for A2 allele type of bulls for breeding purposes. Out of these bulls, only 12 percent were reported to have A1A1 genes, while 48 percent have A1A2 and 40 percent having A2A2 genotype. Among HF bulls, only 22 percent have an A1A1 genotype, 45 percent have A1A2 and 33 percent having an A2A2 genotype. Similarly in Jersey bulls, 60 percent was found A1A2 genotype, 37.5 percent A2A2 genotype and only 2.5 percent population having A1A1 genotype. Interestingly, in crossbred bulls, only 1 per cent A1A1 type of genotype was found, while 50 percent had A2A2 and 49 percent were A1A2 genotypes. Hence, if we are to assume that A1 milk is harmful, there are fewer chances of incidence of diseases because the crossbred cows population in India produced fewer percent of A1A1 genotype of milk. But, till now marketing and trade flourish based on A1 and A2 types of milk by certain companies. Therefore it is imperative to say the onus is on to the policymaker of the country to take an unbiased stand on the issue of A1 and A2 type of milk.

5. Effect of A1/A2 milk on human health

Milk from dairy cows provides a high-quality source of protein and essential micronutrients like calcium, magnesium, and phosphorus to human beings (Bell *et al.*, 2006). Here, we have to be given special emphasis on A1 and A2 types of milk on the risk of disease incidence. Medical literature reported a positive correlation between the development of cardiovascular disease (CVD) and A1 milk protein intake (McLachlan, 2001). Tailford *et al.* (2003) reported that β-casein A1 is more atherogenic than β-casein A2. Laugesen and Elliot (2003) concordance found a strong correlation with the consumption of A1 cattle milk with of incidence of ischemic heart disease (IHD) and Type 1 Diabetes Mellitus. Swinburn, (2004) claimed that a high intake of milk with A1 increases the chance of diseases.

In western countries mostly milk came from HF, jersey and other breeds that carry the A1 allele had a greater incidence of CVD than other nations having A2 milk intake in the

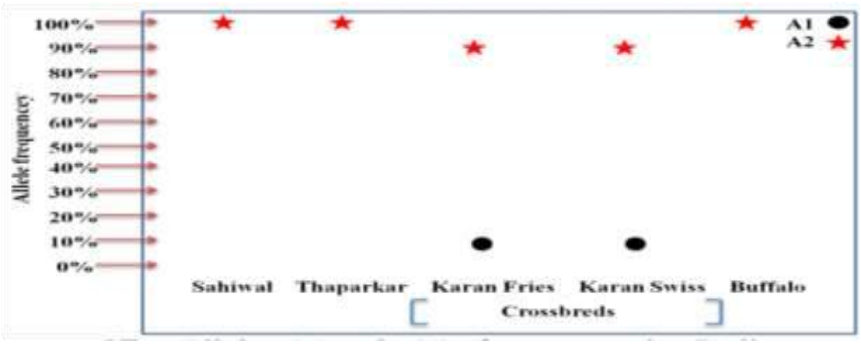

Figure 3. A1 and A2 allele frequency in Indian cattle breeds and crossbreds (Parashar and Saini, 2015)

populations. McLachlan, (2001) also reported that certain communities viz. Masai (East African) and Samburu (Northern Keyan) had virtually no CVD because of consuming milk that carries the A2 allele. Elliot (1992) observed that children in Polynesian islands consuming only A2 type milk were at lesser risk to type 1 diabetes than Polynesian children in Auckland who were consuming A1 type of milk. Kaminski *et al.* (2005) claimed a probable linkage between consumption of A1 milk and the occurrence of ischemic heart disease, sudden infant death syndrome, neurological disorders like autism and schizophrenia in New Zealand. Similar results were also reported by Woodford, (2011) and Mishra *et al.* (2009) on the relationship of A1 milk with many human diseases like CVD, autism, schizophrenia, etc. Laugesen and Elliott (2003) analyzed food consumption data from 19 health care affluent developed countries to study correlations between food consumption and the rates of Type 1 diabetes. Strong correlations (r=0.92) were identified between the consumption of A1 β-casein and the incidence of type 1 diabetes and this incidence was found to be highest in Finland and Sweden countries having the highest A1 β-casein consumption per capita, whereas the lowest A1 β-casein consumption per capita were observed in Venezuela and Japan. Padberg *et al.* (1999) studies antibody response of A1 and A2 β-casein on treatment group (type 1 diabetic patient) and control (no type 1 diabetic patient) and found that A1 β-casein antibodies were significantly ($P<0.001$) higher in treatment groups than the control.

The Food and Agriculture Organisation (FAO, 2012) reported β-casein composition of the protein fraction has become of special interest recently because of a possible relationship between the β-casein genotype and the health of consumers. In the case of Infants chances of rapid absorption of BCM-7 due to the presence of an immature gastrointestinal tract can potentially affect various opioid receptors present in the endocrine, nervous, and immune systems. To date, there is a clear-cut health benefit to consuming A2 milk that is unknown and requires further investigation unlike to harmful effects of A1 milk.

6. Opportunity for Commercialization of A2 Milk

There is an enormous possibility for the commercialization of A2 milk globally since the demand for safe and sound A2 milk is increasing. The A2 Corporation Ltd. (A2C) currently renamed as a2 milk company ltd has been launched to commercialize A2 milk in New Zealand. Further, this company has propagated the business on a huge scale in the name of A2TM in countries of New Zealand, Australia, the United States and Asia (http://www.a2corporation.com). India is auspiciously bestowed with a large number of dairy bovines producing A2 milk. Therefore, demand for Indian cattle and buffaloes milk (A2 milk) is rising globally in countries like Australia, South America, Africa, Brazil, and Southeast Asia (De *et al.,* 2015). So there is a very good opportunity to improve and conservation of A2 type of bovine germplasm for production and selling of A2 milk at a premium price.

6. Conclusion

As stated above, there are many scientists reported that due to consumption of A1 milk produced negative health impacts i.e., diabetes, coronary heart disease, etc. However, other studies by the European food safety authority (EFSA) could not find any relationship between oral intake of BCM-7 and the etiology of such diseases. The Australian and New Zealand food safety Authorities have also reported no correlation between consumption of A1 or A2 milk with diabetes and Coronary Heart Disease incidence. However, to establish the health benefits of A1 vs A2 milk, need to explore more research to sketch a conclusion on the hypothesis. Hence, there is a need to carry forward further research to establish the association between A1 or A2 milk with the etiology of the above-said diseases.

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