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Effect of Honey Supplementation on Plasma Levels of Short Chain Fatty Acids in Malnurished Children

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Abstract

Background: Malnutrition in children is a global public health problem with wide implications. It is estimated that malnutrition is the underlying cause of 45% of global deaths in children below 5 years of age. Honey, has antioxidant, antimicrobial, immunomodulator and anticancer effects. Additionally, honey is appropriate synbiotic combinations can be more effective in benefiting the host than individually administering probiotic or prebiotic.

Aim of Study: To evaluate effect of honey supplementation on plasma levels of short chain fatty acids in Malnurished childrenand to evaluate honey supplementation on malnurished infants and children regarding anthropometric measurements.

Material and Methods: An interventional study. Forty patients of both sexes, aged 6 months to 2 years, were randomizally collected into two equal groups [intervention group 20 patients] and [control group 20 patients]. The study was conducted at Children Hospital of Ain Shams University, Cairo, Egypt during the period from 2018 to 2019. The grading of malnutrition was based on WHO z-score. The dietary intervention consisted ofhoney in a dose of 2ml/kg/day for 8 weeks. Main outcome measures: Evaluate effect of honey supplementation on malnourished children regarding plasma levels of short chain fatty acidsand anthropometric measurements.

Results: Honey consumption in a group of malnourished children resulted in a positive effects as improving anthropometric measures and increase short chain fattyplasa levels.

Conclusion: Honey intervention in a group of children with moderate to severe malnutrition resulted in positive effects on Short Chain Fatty Acids (SCFAs) plasma levels andanthropometric measures, further studies that include a larger number of patients are recommended toconfirm that honey, has beneficial effects, as a complementary agent, in children with Malnutrition.

Key Words: *Honey – Short chain fatty acids – Malnutrition.*

Inroduction

MALNUTRITION is a broad term that encompasses many different manifestations of inadequate nutrition, including both undernutrition and obesity. It is characterized by an imbalance in energy intake and energy expenditure [1]. Pediatric malnutrition (under nutrition) is defined as an imbalance between nutrient requirement and intake, resulting in cumulative deficits of energy, protein, or micronutrients that may negatively affect growth, development, and other relevant outcomes [2,3].

Early childhood malnutrition or under nutrition may lead long-term effects like impairment of gross and fine motor skills, easy fatigue, loss of flexibility, impaired rapid sequence movements, behavioral problems, and cognitive impairment like lower attention spans, language impairment, learning disabilities, and low IQscores [4]. Malnutrition is synonym of undernutrition and results from disease-related deprivation or malabsorption of nutrients, leading to altered body composition. It is quite distinct from disease-free malnutrition, which is related to hunger, socioeconomicand psychologic-related conditions and does not include failure to thrive, defined as a deficient weight gain and related to chronic conditions [5]. Compared with well-nourished children, children with moderate acute malnutrition have a threefold increased risk of mortality and impaired physical and cognitive development. Children with severe acute malnutrition have a ninefold increased risk of mortality [6].

Certain childhood diseases have been associated with microbiome alterations, namely necrotizing enterocolitis, infantile colic, asthma, atopic disease, gastrointestinal disease, diabetes, malnutrition, mood/anxiety disorders, and autism spectrum disorders. Treatment studies suggest that probiotics are potentially protective against the development of some of these diseases [7].

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Gut microbial fermentation products Dietary carbohydrates, along with proteins and peptides which escape from the host upper gut digestive enzymes, are fermented by the microbiota in the cecum and the colon [8]. The intestinal microbiota contributes to the defense against pathogens by the mechanism of colonization resistance and fermentation of nondigestible carbohydrates, occurring mostly in the proximal colon. The main products produced by are Short Chain Fatty Acids (SCFAs). Butyrate is a major energy source for intestinal epithelial cells; affects cell proliferation, cell differentiation, mucus secretion, and barrier function; and has anti-inflammatory and antioxidative potential. Hence, the gut microbiota performs a wide variety of metabolic activities that are essential for the host's metabolism [9].

SCFAs are the principal metabolites of gut microbiota, which have several important physiological roles in maintaining the host healthy. These metabolites act as intermediators between gut microbiota and host to regulate intestinal permeability, inflammation control, and bile acid metabolism, immunological functions, and disease control. Regardless of their normally low concentration in the peripheral bloodstream, propionate and butyrate affect organs indirectly by activation of hormonal and nervous systems. For instance, butyrate is a vital energy source for colonic epithelial cells, and the maintenance of colonic homeostasis; butyric acid is also a histone deacetylase inhibitor, through which it regulates gene expression and cell fate. Propionic acid acts as an inhibitor of fatty acid production in humans, and as a low-grade inflammation reducing agent in the gut. SCFAs reduces the risk and symptoms of many metabolic and inflammatory diseases, including Inflammatory Bowel Disease (IBD), cardiovascular disease, colorectal cancer (CRC), obesity, and diabetes [10].

The effects of SCFAs in the intestines and elsewhere are derived from their ability to stimulate three G-protein coupled receptors (GPRs), GPR41, GPR43, and GPR109a, as well as their ability to act as Histone Deacetylase Inhibitors (HDACi) [11].

It is important to note that fecal SCFA concentrations do not reflect their concentration and production rate in the intestine as most SCFAs are taken up by the host and therefore fecal SCFA excretion provides little information about actual intestinal SCFA metabolism [12]. The fecal content of SCFAs does not directly correlate with the rate at which acetate, propionate, or butyrate are metabolized. In addition, propionate and butyrate have the capacity to activate intestinal gluconeogenesis [13].

"Natural or processed foods that contain biologically active compounds which, in defined effective, and non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers for the prevention, management, or treatment of chronic disease or its symptoms" The Functional Food Center (FFC) definition of "functional foods" [14].

Synbiotics are defined as a mixture containing both prebiotics and probiotics, more specifically where the prebiotic compound aids the growth of the beneficial probiotic bacteria in the host. Also as products that contain both probiotics and prebiotics [9-15].

The stimulation of probiotics with prebiotics results in the modulation of the metabolic activity in the intestine with the maintenance of the intestinal biostructure, development of beneficial microbiota, and inhibition of potential pathogens present in the gastrointestinal tract. Synbiotics may confer additional benefits over a probiotic by increasing bifidobacteria levels in the intestine [16].

Prebiotics are used mostly as a selective medium for the growth of a probiotic strain, fermentation, and intestinal passage. A probiotic is essentially active in the small and large intestine, and the effect of a prebiotic is observed mainly in the large intestine. It has been reported that, due to the use of prebiotics, probiotic microorganisms acquire higher tolerance to environmental conditions, including oxygenation, pH, and temperature in the intestine of a particular organism. Hence, the combination of the two is expected to have a synergistic effect. Action through the improved viability of probiotic microorganisms and action through the provision of specific health effects [17].

Honey is a natural substance with a lot of benefits for nutrition and health. Among honey benefits are its anti-inflammatory, anti-oxidant and antimicrobial effects and knowing the pathogenesis of PEM such patients are expected to benefit from honey [18].

The most important ingredient of honey is carbohydrates present in the form of monosaccharides, fructose, glucose and disaccharides, maltose, isomaltose, maltulose, sucrose and turanose and the sweetness of honey is due to presence of these ingredients. It also contains oligosaccharides including the anderose and panose and enzymes including amylase, oxidase peroxide, catalase and

acid phosphorylase. Furthermore, honey contains amino acids, trace vitamin B, Vitamin B6, Vitamin C, niacin, folic acid, minerals, iron, zinc and antioxidants **[19]**.

Honey oligosaccharides had a potential prebiotic activity. These compounds selectively stimulate the growth of beneficial microorganisms, such as Lactobacillus and Bifidobacterium. Honey oligosaccharide affects the bacteria population in human Gut Intestinal Track (GIT) and found honey that contain higher amount of oligosaccharide resulted in large amount of beneficial bacteria's growth **[19]**.

Most of the antioxidant compounds present in honey affect the viability of a series of undesirable microorganisms but does not affect probiotic bacteria or, in many cases, even stimulate their growth or activity **[20]**.

Patients and Methods

Type of the study: This study was intervention study.

Subjects: This study conductedon 40 patients of both genders aged 6 months to 2 years; with moderate to severe malnutrition according to WHO z-scoresdivided into 2 groups the honey group (intervention group) and the control group. Rrecruited from the Nutrition Clinic of the Pediatric Hospital, Ain Shams University, Egypt during the period from 2018 to 2019. The patients were randomly assigned following a simple randomization procedure (computerized random numbers) to either the honey (group 1) or the control group (group 2) with a 1:1 allocation ratio. Each group consisted of 20 patients.

Inclusion criteria: Age: 6 months-2 years of both gender, diagnosed with moderate to severe malnutrition according to WHO standards and definitions (the diagnosis of the undernutrition is due to inadequate energy intake).

Diagnosis of malnutrition according to WHO definitions:

1- Mild malnutrition as a z-score –1 to –1.9.
2- Moderate malnutrition a z-score between –2 and –2.9.
3- Severe malnutrition a z-score <–3.

Exclusion criteria: The exclusion criteria included markedly ill patients, and children with chronic or severe systemic illness, including cancer, sepsis, endocrine disorders, neurologic disorders, diabetes mellitus, and children with heart, renal or liver cell failure. Also, any child, in whom the undernutrition is caused by diseases or conditions that interfere with nutrient intake or their use by the body such as malabsorption disorders, chromosomal aberrations, inborn errors of metabolism, malabsorption syndrome or diseaseand chronic diarrhea, food allergy were excluded.

Methods: Ethical considerations: The study protocol was approved by the Pediatric Department Board of Ain Shams University. An informed consent was obtained from each patient and control legal guardians before enrollment in the study.

All participants were subjected to the following: History taking with special emphasis on the: Dietetic history, history of any disease that might interfere with the nutrient intake or their metabolism by the body, history of acute or chronic illness.

Clinical examination laying stress on: Complete physical examination for each participant during the study.

Anthropometric measurements: Body Weight measurements (BW), Body Length measurements (BL), Head Circumference (HC), Mid-arm circumference (MUAC) **[21]**.

Honey intervention: Each patient in the intervention group or honey group or (group 1) took oral honey in a dose of 2ml/kg/day for 8 weeks. This dose of honey was empirical because there was no identification of a particular dose of honey in earlier clinical trials using honey in different diseases, and the oral dose of honey used for infants and children in previous clinical trials ranged from 0.5 to 2ml/kg/day **[19,20,22,23]**. Moreover, dose-related toxicity to honey has not been previously reported. Also, recommended honey doses are not required for safety purposes **[24]**.

The calculated dose of honey was dissolved in water with a ratio of 1:3, respectively, and then ingested by the patient before breakfast.

Dissolving honey in water enhances its antimicrobial properties **[25]**, facilitates swallowing and helps adjusting the dose. The honey used in this study was a raw, unprocessed (not heated or irradiated) clover honey that was supplied directly from an apiary located in Al Mahala-Gharbia Governorate, Egypt, and then kept at room temperature away from light until being consumed by the patient.

Microscopic examination of samples from honey confirmed the presence of pollen grains, which were mainly of clover (Trifoliumalexandrinum).

The honey was also tested for the presence of Clostridium botulinum spores before use (no spores were detected). Examination of honey for C. botulinum spores was done by centrifugation and filtration of the supernatant, followed by culture on cooked meat **[26]**.

Each participant in the honey group was provided by 7 glass containers each week. Each container contained the calculated daily dose of undiluted honey; to be dissolved in water just before being ingested before breakfast. The parents or care-givers were instructed to keep the containers well closed and away from light until the time of administration before breakfast every day. They were also instructed not to give any additional doses of bee honey to their children during the study. Also, the parents or the care givers of the malnourished control group or group 2 were instructed not to give bee honey to their children during the study period.

The caloric value of each dose of honey was subtracted from the total daily caloric intake of infants and children.

Laboratory: Study tools: Plasma SCFAs levels were measured by HPLC before and after intervention.

Results

The present study included 2 groups of 40 patients were diagnosed with moderate to severe malnutrition according to WHO z-scores divided into 2 groups the honey group (intervention group) and the control group. With the same inclusion and exclusion criteria.

Table (1): Baseline characteristics (demographic data, anthropometric measurements and pre intervention short chain fatty acid plasma levels) of the study groups (honey group and control group).

		Intervention Group (n=20)	Control Group (n=20)	Test	*p*-value
Demographic data:					
Age (months):	Mean ± SD	18.90±3.63	16.15±4.92	*t*=1.011	0.142
	Range	12-24	9-22		
Sex:	Male	12 (60.0%)	9 (45.0%)	χ^2=0.902	0.342
	Female	8 (40.0%)	11 (55.0%)		
Residence:	Urban Area	14 (70.0%)	10 (50.0%)	χ^2=1.667	0.197
	Rural Area	6 (30.0%)	10 (50.0%)		
Pre anthropometric measurements:					
Weight (Kg):	Mean ± SD	7.53±1.08	7.00±0.95	1.646	0.108
	Range	5.5-9	5.5-9		
Wt for age Z score:	Mean ± SD	–3.19±0.85	–3.04±0.82	–0.563	0.576
	Range	–4.57–-1.40	–4.3 8–-1.44		
Height (cm):	Mean ± SD	72.28±6.09	68.59±5.00	1.093	0.116
	Range	62.5-88	60-78		
Ht for age Z score:	Mean ± SD	–4.63±2.25	–3.72±1.21	–1.597	0.119
	Range	–7.79–-0.90	–6.44–-2.38		
Wt for Ht Z score:	Mean ± SD	–0.85±2.25	–1.36±1.31	0.868	0.391
	Range	–5.42-3.20	–3.27-1.82		
MUAC:	Mean ± SD	11.43±0.46	11.12±0.39	1.308	0.387
	Range	10.5-12.4	10.5-12		
HC:	Mean ± SD	47.81±1.32	46.77±1.91	1.990	0.084
	Range	45.5-50	43.5-50.5		
BMI [wt/(ht)^2] :	Mean ± SD	14.18±1.48	15.06±2.02	–1.570	0.125
	Range	10.9-16.3	12.6-19.4		
Pre short chain fatty acids (microgram/ml):					
Formic acid (microgram/ml):	Mean ± SD	18.94±26.44	19.63±16.96	1.461	0.144
	Median (IQR)	7.61 (11.97)	15.33 (20.13)		
	Range	3.29-98.8	2.79-62.17		
Acetic acid (microgram/ml):	Mean ± SD	43.84±71.91	72.97±123.14	0.054	0.957
	Median (IQR)	21.27 (36.55)	20.64 (71.33)		
	Range	3.22-321.4	3.6-509.02		
Butyric acid (microgram/ml):	Mean ± SD	77.82±124.27	75.20±96.09	1.467	0.256
	Median (IQR)	24.95 (50)	22.65 (105.74)		
	Range	3.73-166.5	9.77-369.34		

Table (1) shows that there was no statistically significant difference between honey group and control group according to pre intervention with honey supplementation regarding to baseline characteristics.

Table (2) shows that, statistics shows significant increase in weight (p-value 0.0 11), weight for age z-score (p-value 0.0 16), weight for height z-score was highly significant (p-value 0.036) and a highly significant Body Mass Index (BMI) (p-value <0.001). Also shows there were no statistically significant increase regarding to height, height for age z-score, MUAC and head circumference between honey group and control group after honey supplementation.

Table (2): Comparison between honey group and control group according to post anthropometric measurements.

Post anthropometric measurements	Honey Group (n=20)	Control Group (n=20)	*t*-test	p-value
Weight (Kg):				
Mean ± SD	9.46± 1.52	8.28± 1.28	2.671	0.011*
Range	6.5-12	6-12		
Wt for age Z score:				
Mean ± SD	–1.06±0.91	–1.85± 1.07	2.533	0.016*
Range	–3.138-–0.024	–4.652-–0.112		
Height (Cm):				
Mean ± SD	74.18±6.59	70.28±5.02	1.105	0.419
Range	65-91	62.6-80		
Ht for age Z score:				
Mean ± SD	–3.75± 1.72	–3.66± 1.16	–0.193	0.848
Range	–6.02-1.27	–6.48-–2.33		
Wt for Ht Z score:				
Mean ± SD	–0.70± 1.12	–1.15±0.83	2.162	0.036*
Range	–1.938-1.327	–2.5-0.931		
MUAC:				
Mean ± SD	12.08±0.71	11.76±0.46	1.683	0.101
Range	11-13.4	10.9-12.4		
HC:				
Mean ± SD	47.48±7.17	48.67±2.00	–0.718	0.477
Range	17.5-51	44.5-52.3		
BMI [wt/(ht)^2]:				
Mean ± SD	19.19± 1.55	17.03± 1.75	4.129	<0.001**
Range	15.72-21.8	13.48-19.1		

t: Independent Sample *t*-test. * : p-value <0.05 S.
p-value >0.05 NS. **: p-value <0.001 HS.

Table (3): Comparison between honey group and control group at the end of the study regarding to Short Chain Fatty Acids (SCFAs) plasma levels.

Post short chain fatty acids (Microgram/ml)	Honey Group (n=20)	Control Group (n=20)	Z-test	p-value
Formic acid (Microgram/ml):				
Mean ± SD	61.03±45.96	37.22±67.79	2.273	0.023*
Median (IQR)	55.42 (89.47)	20.62 (24.04)		
Range	5.19-146.88	4.47-320.1		
Acetic acid (Microgram/ml):				
Mean ± SD	70.48±65.30	30.65±27.30	2.300	0.021*
Median (IQR)	59.88 (52.65)	19.47 (43.75)		
Range	5.5-223.65	2.4-89.61		
Butyric acid (Microgram/ml):				
Mean ± SD	97.01±66.44	80.15±57.19	4.483	0.011*
Median (IQR)	68.80 (71.41)	29.92 (74.02)		
Range	4.09-234.15	5.46-176.93		

Z: Mann-Whitney test. p-value >0.05 NS. *: p-value <0.05 S.

Table (3) shows that, there was a significant statistically increase in Formic acid (p-value 0.023), Acetic acid (p-value 0.021) and Butyric acid (p-value 0.011) between honey group and control group after honey supplementation.

Table (4) shows that, there was a significant statistically increase according to the rate of the change % regarding to Acetic acid plasma level (p-value 0.033), Formic acid (p-value 0.033) and Butyric acid (p-value 0.035) between honey group and control group.

Table (5) shows that,there was a significant increase in Short Chain Fatty Acid plasma level regarding to formic acid (p-value 0.008), Acetic acid (p-value 0.021) and Butyric acid (p-value 0.017) between pre intervention and post intervention with honey supplementation in the honey group.

Table (4): Comparison between honey group and control group according to rate of change % regarding to short chain fatty acids plasma levels.

Rate of change% short chain fatty acids (Microgram/ml)	Honey Group (n=20)	Control Group (n=20)	Z-test	p-value
Formic acid (Microgram/ml):				
Mean ± SD	965.54±756.55	282.63±383.75	3.682	0.013 *
Median (IQR)	371.72 (1077.19)	67.45 (283.81)		
Range	–67.54-4224.32	–92.81-2794.21		
Acetic acid (Microgram/ml):				
Mean ± SD	353.16±624.78	101.99±343.32	2.138	0.033*
Median (IQR)	103.12 (304.59)	–49.25 (176.38)		
Range	–94.56-2392.55	–91-1365.56		
Butyric acid (Microgram/ml):				
Mean ± SD	24.65±117.94	6.58±156.27	2.975	0.035*
Median (IQR)	25.64 (70.2)	6.80 (44.78)		
Range	–85.46-2636.46	–86.24-2131.62		

Z: Mann-Whitney test. p-value >0.05 NS. *: p-value <0.05 S.

Table (5): Comparison between pre intervention and post intervention according to short chain fatty acids plasma levels in the honey group (n=20).

Short chain fatty acids (Microgram/ml)	Pre intervention (n=20)	Post intervention (n=20)	Change	Z-test	p-value
Formic acid (Microgram/ml):					
Mean ± SD	18.94±26.44	61.03±45.96	42.08±58.65	2.651	0.008 *
Median (IQR)	7.61 (11.97)	55.42 (89.47)	39.63 (96.6)		
Range	3.29-98.8	5.19-146.88	–46.57-140.26		
Acetic acid (Microgram/ml):					
Mean ± SD	43.84±71.91	70.48±65.30	26.63±96.54	2.315	0.021*
Median (IQR)	21.27 (36.55)	59.88 (52.65)	22.54 (59.14)		
Range	3.22-321.4	5.5-223.65	–243.14-185.80		
Butyric acid (Microgram/ml):					
Mean ± SD	77.82±124.27	97.01±66.44	19.19±73.26	3.741	0.017*
Median (IQR)	24.95 (50)	68.80 (71.41)	27.36 (92.47)		
Range	3.73-166.5	4.09-234.15	–368.59-98.34		

Z: Wilcoxon test. p-value >0.05 NS. *: p-value <0.05 S.

Discussion

Malnutrition usually associated with poor socioeconomic conditions, poor maternal health and nutrition, frequent illness, and/or inappropriate infant and young child feeding and care in early life. Stunting holds children back from reaching their physical and cognitive potential **[21]**.

The formation of SCFA is the result of a complex interplay between diet and the gut microbiota within the gut lumen environment **[27]**. Identifying the pharmacological targets and signalling properties of these gut microbial metabolites is vital for understanding the underlying mechanisms of the gut-microbial metabolites-host interaction in modulating host's cellular functions. As these metabo-

lites have been shown to interfere with host metabolism via several mechanisms, including acting as signalling molecules activating intracellular signaling cascades, three classes of gut microbial metabolites that play important roles in host molecular mechanisms: Short-Chain Fatty Acids (SCFA), methylamines, and indoles **[28]**.

"Natural or processed foods that contain biologically active compounds which, in defined effective, and non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers for the prevention, management, or treatment of chronic disease or its symptoms" The Functional Food Center (FFC) definition of "functional foods" **[15]**.

Our aim of the work was to evaluate effect of honey supplementation on malnurished children regarding anthropometric measurements and plasma levels of short chain fatty acids.

To our knowledge, this study may be the first study that correlates between honey supplementation and plasma levels of short chain fatty acids in malnourished children.

The present study was done on 40 patients with moderate to severe malnutrition according to WHO z-scores (WHO 2012 and 2013) divided into 2 groups the honey group (intervention group) and the control group.

At baseline, the two studied groups were comparable as regards the demographic data (age, sex, residenceand educational level of the parent). Also, the study groups 1 and 2 were matched as regards the Short Chain Fatty Acids plasma levels and the anthropometric measures and their Z scores. As expected, the anthropometric measures were significantly low in the honey group and the control groupas the inclusion criteria required diagnosis with moderate to severe malnutrition according to WHO z-scores.

Both childhood undernutrition and obesity are linked to alterations in composition and functionality of the gut microbiome. One of the possible mechanisms underlying the interplay between microbiota and host metabolism is through appetite-regulating hormones (including leptin, ghrelin, glucagon-like peptide-1). Short chain fatty acids, the end product of bacterial fermentation of non-digestible carbohydrates, might be able to alter energy harvest and metabolism through enteroendocrine cell signaling, adipogenesis and insulin-like growth factor-1 production. Elucidating these mechanisms may lead to development of new modulation practices of the gut microbiota as a potential prevention and treatment strategy for childhood malnutrition **[5]**.

As a possible effect of honey supplementation, statisiticshows significal increase in weight (p-value 0.011), weight for age z-score (p-value 0.016), weight for height z-score (p-value 0.036) and a highly significan Body Mass Index (BMI) (p-value <0.001) by the comparison between the honey group (group 1) and the control group (group 2) who did not receive honey, the positive effect of honey on the anthropometric measures in Protein Energy Malnourished (PEM) patients was also observed in the study of Shaaban et al. **[17]**.

Among various microbiota metabolites important in regulation of host physiology and health, SCFAs (including acetate, propionate, and butyrate) are derived from the bacterial fermentation of dietary fibers, which escape absorption in the small intestines and enter into the colon. Acetate is the most abundantly produced SCFA, followed by propionate and butyrate in a 3:1:1 molar ratio. SCFA formation is dictated by both the type of bacteria and type of dietary fiber present in the colon **[16,29]**.

Possible effect of honey supplementation Comparing the Short Chain Fatty Acids (SCFAs) plasma levels in the two malnourished groups 1 and 2, after 8 weeks of nutritional rehabilitation and honey intervention in honey group, was that statistics showed significal increase in Formic acid (p-value 0.023) and changing in plasma level mean from (18.94±26.44) to (61.03±45.96) and Acetic acid (p-value 0.021), changing in plasma level from (43.84±71.91) to (70.48±65.30) and Butyric acid plasma level (p-value 0.011) changing in plasma level mean from (77.82±124.27) to (97.01±66.44) between honey group and control group. While in the control group the mean of plasma level of Formic acid changed from (19.63±16.96) to (37.22± 67.79), the Acetic acid plasma level from (43.84 ± 71.91) to (30.65±27.30) and Butyric acid mean from (75.20±96.09) to (80.15±57.19) who received only nutritional rehabilitation.

Favarin et al., **[30]** reported that addition of honey as an encapsulant improved the survivability of two probiotic Bifidobacterium strains in simulated GI conditions, and the protective effect was comparable to sodium alginate microencapsulation.

Also our study showed correlation between change short chain fatty acids (Microgram/ml) with change anthropometric measurements in hney-group as the results showed significant positive

correlation between change formic acid and BMI (p-value 0.017), also significant between acetic acid with weight (kg) (p-value 0.032), wt. for age z-score (p-value 0.046) and height for age z-score (p-value 0.044).

The honey has prebiotic effect by stimulating the growth and activity of probiotic bacteria. Besides, because of osmotic constitution and composition of the honey, it acts as protectant to the passage of probiotic bacteria throughout gastrointestinal tract. In fact, honey has three functions related to probiotics aspects: It may contain probiotic microorganisms itself, prebiotic substances and protective function to probiotics during the transit by gastro-intestinal conditions **[21]**.

Conclusion:

8 weeks of honey consumption in a group of malnourished children resulted in such positive effects as improving anthropometric measures and increase Short Chain Fatty plasma levels.

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تأثير مكملات العسل على مستوى الأحماض الدهنية قصيرة السلسلة فى الدم لأطفال يعانون من سوء التغذية

هذه الدراسة دراسة تداخلية حيث أنها شملت أربعين طفلاً تم إختيار المرضى بطريقة عشوائية مبسطة بنسبة ١:١ حيث أنه تم جمع أربعين مريضاً مقسمين إلى مجموعتين تتضمن كل مجموعة ٢٠ مريضاً المجموعة الأولى وهى مجموعة العسل التى سوف يتم التدخل معها بمكملات العسل والمجموعة الثانية وهى مجموعة المراقبة. تتضمن شروط إختيار المرضى أن يكونوا قد تم تشخيصهم بسوء التغذية من الدرجة المتوسطة إلى الدرجة الحادة وفقاً لمعايير منظمة الصحة العالمية وأن يتراوح عمرهم من الستة أشهر إلى العامين من كلا الجنسين. كل مشارك فى مجموعة العسل قد تلقى العسل يومياً ولمدة ثمانية أسابيع وفقاً للجرعة التى قد تم حسابها وهى ٢مجم لكل كيلوجرام فى اليوم وذلك مع التنبيه على أن يتم دمجها بالماء بنسبة ١:٣ ليتم أخذها يومياً قبل الإفطار. قد تم المقارنة المبدئية بين المجموعتين قبل البدء بالتدخل بمكملات العسل من حيث الخصائص الديموغرافية (السن – الجنس ومكان المعيشة). أيضاً قد تم المقارنة بين المجموعتين من حيث مستوى الدهون قصيرة السلسلة فى بلازما الدم. نسبة إلى القياسات الأنثروبومترية وبعد ثمانية أسابيع من التدخل بالعسل فى مجموعة العسل بالمقارنة مع مجموعة المراقبة حيث أنه قد تم ملاحظة الإختلاف إرتفاع النسبة الإحصائية للوزن (كجم) بمعدل (p-value <0.001)، وبالنسبة إلى الوزن بمعدل (Z-score p-value 0.005).

معدل أعلى محيط الذراع (p-value <0.001) ومعدل الطول (p-value <0.001) وكان معدل المقارنة بالنسبة لمؤشر كتلة الجسم وأوضح ذلك الإختلاف لمجموعة العسل بالنسبة إلى الوزن والطول ومعدل الوزن إلى العمر ومؤشر كتلة الجسم ومحيط أعلى الذراع بالمقارنة مع مجموعة المراقبة. أيضاً قد تم تسجيل زيادة فى قياسات الدهون قصيرة السلسلة فى البلازما بالنسبة لمجموعة العسل بالمقارنة مع مجموعة المراقبة حيث وفقاً لمتوسط لحمض الفورميك حيث أنه كان قبل التدخل (18.94±26.44) ثم أصبح بعد التدخل (61.03±45.96) مع قيمة (p-value (0.008)، وتم تغير متوسط حمض الآستيك من (26.63±96.54) ليصبح بعد التدخل (43.84±71.91) بقيمة (p-value (0.021) وكان معدل حمض البيوتريك حيث أنه تم تغيير متوسطه من (24.65±117.94) إلى (77.82±124.27) بقيمة (p-value (0.017*).