Assessment the concentration of malondialdehyde MDA and polyubiquitin C Protein in patients with Breast and Gastric Cancer

Evaluación de la concentración de malondialdehído MDA y proteína poliubiquitina C en pacientes con cáncer de mama y gástrico

Saleen Salam Abdulhadi[1], Prof. Dr. Abbas Abdullah Mohammad[2], Ammar Adil Jasim*[3]
[1]Central Organization for Standardization and Quality Control (COSQC)/Ministry of Planning./Iraq. Saleen.salam86@gmail.com;
[2]Biotechnology Branch / Applied Sciences Department /University of Technology/Iraq. Abbas2019@gmail.com
[3]Department of Biochemistry, College of Medicine, University of Baghdad/Iraq. ammar.a@comed.uobaghdad.edu.iq;
Received/Recibido: 04/21/2021 Accepted/Aceptado: 05/15/2021 Published/Publicado: 06/10/2021 DOI: http://doi.org/10.5281/zenodo.5651770

Abstract

Background: Nowadays, overweight and obesity amongst children is regarded as an increasingly concerning health problem in the majority of countries. Patients and methods: Ninety-six cases participated in the present survey, twenty-seven were less than six years, and sixty-nine were 6-18 years. They all had a BMI of more than 95% for their age and gender; they were clinically assessed as overweight children. History, physical testing, and examining the most related laboratory tests were conducted to consent acquisition. Results: It is observed that there is a substantial variation in the average age group of the two groups, hypercholesterolemia and high triglyceride were more recorded between cases older than six years. Iron deficiency anemia and asthma were reported as more substantially connected to the younger group (<6 years). Liver enzyme abnormalities, gall stones, musculoskeletal pain did not demonstrate any statistical distinction between the two groups.

Keywords: The burden of obesity; children health.

Resumen

Antecedentes: Hoy en día, el sobrepeso y la obesidad entre los niños se considera un problema de salud cada vez más preocupante en la mayoría de los países. Pacientes y métodos: Noventa y seis casos participaron en la presente encuesta, veintisiete tenían menos de seis años y sesenta y nueve tenían entre 6 y 18 años. Todos tenían un IMC de más del 95% para su edad y sexo; fueron evaluados clínicamente como niños con sobrepeso. Se llevaron a cabo la historia, las pruebas físicas y el examen de las pruebas de laboratorio más relacionadas para obtener el consentimiento. Resultados: Se observa que existe una variación sustancial en el grupo de edad promedio de los dos grupos, registrándose más hipercolesterolemia y triglicéridos altos entre los casos mayores de seis años. Se informó que la anemia por deficiencia de hierro y el asma se relacionaron más sustancialmente con el grupo más joven (<6 años). Las anomalías de las enzimas hepáticas, los cálculos biliares, el dolor musculoesquelético no demostraron ninguna distinción estadística entre los dos grupos.

Palabras Clave: La carga de la obesidad; salud infantil.

Introduction

Childhood obesity is an escalating health issue in both developed and developing countries sparing only regions with chronic deprivation[1,2], it's one of the prominent confront of the 21 century[3].

Obesity among children is allied to earnest complication that embrace a high chance of ill health and early death[4].

Actually it may even threaten health of children and may persist to have adverse influence to adulthood[5,6]. The modern way used to assort persons as (obese) is by Body Mass Index BMI), as it estimates adipose tissue and body fat bulk, it is delineated by the ratio of weight in kilograms) to the square meter of height (meters)[7].

In accordance with CDC guidelines that determined at 2008, BMI of pediatric age group alter with their growth consequently chart of their age and gender were accustomed[8].

In pediatric age group the joining of adiposity "true fat deposition "to BMI may be less tight than adult. there-

fore, they are outlined as obese when their BMI seem above their specific centile for age and gender[9].

During childhood period, levels of body fat alter starting with high level during infancy then decrease to about 5.5 years until the period termed adiposity rebound, as body fat is naturally at nadir level but then increases until early adulthood. Hence, obesity and overweight are determined by using BMI percentiles[10].

Children older than 2 years old with a BMI ≥95th percentile join the criteria for obesity, while those with a BMI between the 85th and 95th percentiles termed as overweight[10] this were recently assorted by the institute of medicine[11].

Obesity is considered a sophisticated multifactorial health problem that influenced by many genetic and environmental points[12,13].

It is well known that increment in obesity is a result of poor balance between intake and expenditure, this had been hardly joined to life style assumed and dietary habits[14]. High caloric diet, sedentary life style, television watching in addition to overuse of electronic games has been blamed to the rising in obesity prevalence in the recent years[15-17].

Monitoring and control of food intake arise by neuroendocrine feedback system joining adipose tissue, central nervous system and gastrointestinal tract[10].

Genetic determinants may play a role in adiposity such as FTO gene blamed in aiding increasing intake. 10 Genetic vulnerabilities often require to be joined with associated environmental personal behavior to affect weight[14].

Many genetic syndromes are also associated with this problem such as prader-willi and ROHHAD syndrome[10].

Many organic causes are also blamed like hypothyroidism, cushing syndrome, GH deficiency, hyperinsulinism and pseudohypoparathyroidism[10,18].

Many prenatal influence affect obesity including maternal obesity and maternal smoking, gestational diabetes, large for gestational age[19]. Breast feeding is considered modestly protective[20,21].

Hispanic and south Asia, children from urban areas have a higher risk for overweight and obesity[22-24].

Females are also at higher risk of obesity than males secondary to their hormonal status[25]. Those with low and mid socioeconomic status are also at higher risk[26-28].

A suggestion about the role of microbial infection in obesity, adeno virus Ad 36 infection and the gut composition (ratio of firmiculate to bacteroid) are suggested to have an associate[29].

Depression can be a cause or a result of obesity[30]. Obesity among children can intensely affect their emotional, physical and social well-being. It's also affect their self-esteem[31]. Poor academic achievements are also seen frequently among them[32].

Comorbidities are seen during childhood and adolescence; it's also persist to adulthood. There is higher morbidity and mortality among those patient which raise the importance of prevention and treatment[10].

Type 2 DM, hyperlipidemia, hypertension and non-alcoholic fatty liver disease are immediate complications. Insulin resistance aids adiposity and affects lipid metabolism causing cardiovascular disease[33,34].

Hypertension and dyslipidemia were seen 8.5 folds more among overweight than lean children[35].

OSA was seen 6 folds more among obese children than non-obese.[36] asthma prevalence is also more reported among obese[37] other comorbidities are gall stone, sleep apnea, asthma, nutritional deficiency and some orthopedic problems. there is also a possibility of chronic inflammation secondary to low adiponectin level in those patients[38].

Musculoskeletal pain and Blount disease are well-known orthopedic health problems for them[38].

NAFLD occurs in 10 -25% of them. Liver function test is strongly considered to be obtained for obese patients as they are typically asymptomatic[39,40]. If ATL is two times more than normal for more than 3 months, abdominal US is sometimes mandatory to affirm the diagnosis[39,41].

Socially obesity is considered as a stigmatizing and socially an acceptable condition. patients may be excluded from many activities in particular competitive sports[34].

Management should involve the principles of primary and secondary prevention as primary one is important in prevention of obesity while the secondary is essential to minimize complications[42].

Pharmacotherapy is usually limited to selected patients in particular those with significant morbidities.[42] The only FDA-approved drug for children younger than 16 years is orlistat, which is lipase enzyme inhibitor. It decreases fat absorption and aids weight loss moderately[10].

There are another promising combination (amylin + leptin), the former decreases intake and slows gastric emptying while the other has anorexigenic effect when given as a combination[10].

If insulin resistance is clinically confirmed, Metformin may be prescribed[43,44].

Octreotide for hypothalamic obesity, its used to suppress insulin and stabilize BMI[45,46].

Regarding bariatric surgery, it's should be limited to patients who has complete or near-complete skeletal maturity, has BMI more than or equal to 40, presence of comorbidities, failure of 6 months' trial of weight reducing program[10,47,48].

It may carry many complications that vary from wound infection to life threatening complication such as intestinal obstruction and perforation[10].

Management of comorbid disease is required accordingly[10].

Aims of the study

1. To determine the impact of obesity on children health.

2. To find out any association between these morbidities and age groups.

Methods

Ninety-six patients aged 2-18 years were enrolled in this survey. Twenty-seven of them were less than 6 years and 69 were more than 6 years. all of them had a BMI >95% for age and gender and were clinically diagnosed with obesity.

Data collected over 1-year period from the 1st of November 2018 to the 30th of November 2019.

The patients were identified as part of their need to medical care, most of the families were unaware of their child health problem and many escape the survey and were excluded.

Consent acquisition was obtained for all patients involved, we start with the evaluation of centile charts. Detailed history about family eating habit, level of physical activity, residency, education level and socioeconomic status.

Focusing on clinical sign of comorbid disease, psychological status of the patient, symptom of OSA, asthma, GERD, iron deficiency anemia, musculoskeletal pain, gall bladder disease.

Blood pressure was measured for all patients with appropriate sized cuff. Many lab investigations were performed for all patents such as hemoglobin, serum iron, TIBC, random blood sugar, liver enzymes (ALT, AST), serum cholesterol, serum triglyceride.

Abdominal ultrasound was performed to selected patients (those with abnormal liver function test and patients with symptoms of gall bladder disease).

Statistical analysis

Data were analyzed using statistical package for social science (SPSS) (IBM, Chicago, USA, version 23). Quantitative variables were expressed as mean, range and standard deviation; whereas, qualitative variables were expressed as number and percentage. Independent samples t-test was used to compare mean between two groups, while chi-square test and Yates correction for continuity were used to assess difference in frequency distribution of qualitative variables between groups. The level of significance was set at $P \leq 0.05$ and the level of high significance was set at $P \leq 0.01$.

Results

The demographic characteristics of children enrolled in this study were outlined in table 1. The study included obsess children with body mass index ≥ 95% for age and gender, who were categorized according to age into two groups, the first group included children 6 years or younger and the other group included children who were > 6 years.

There was highly significant difference in mean age between the two groups (P<0.001), no significant difference in gender distribution (P=0.407), significant difference in distribution according to residency (P=0.017), and no significant difference in socioeconomic status (P=0.309), as shown in table 1.

Biochemical abnormalities were shown in table 2. Hypercholesterolemia, hypertriglyceridemia and impaired glucose tolerance were significantly more frequent in obese children more 6 years of age in comparison with children 6 years or less (P<0.001); however, there was no significant difference in the frequency of liver enzyme abnormalities between the two groups (P=0.398), table 2.

Hypertension, psychological abnormalities, sleep apnea, gastroesophageal reflux disease (GERD) were significantly more frequent in obese children more 6 years of age in comparison with children 6 years or less (P<0.001): while asthma and iron deficiency anemia (IDA) were more significant to the younger age group; however, there was no significant difference in the frequency distribution according gall bladder disease and musculoskeletal disorders between both groups (P>0.05), as shown in table 3.

Table 1. Demographic characteristics of obese children enrolled in this study

Characteristic	Age < 6 years n = 27	Age > 6 years n = 69	P
Age (years)			
Mean ±SD	3.93 ±1.24	12.20 ±3.04	< 0.001 † HS
Range	2 -6	7 -18	
Gender			
Male, n (%)	17 (63.0 %)	37 (53.6 %)	0.407 ¥ NS
Female, n (%)	10 (37.0 %)	32 (46.4 %)	
Residency			
Urban, n (%)	14 (51.9 %)	53 (76.8 %)	0.017 ¥ S
Rural, n (%)	13 (48.1 %)	16 (23.2 %)	
Socioeconomic status			
Poor, n (%)	9 (33.3 %)	16 (23.2 %)	0.309 ¥ NS
Good, n (%)	18 (66.7 %)	53 (76.8 %)	

n: number of cases; †: Independent t-test; ¥: Chi-square test; HS: highly significant at P ≤ 0.01; NS: Not significant at P > 0.05; S: significant at P ≤ 0.05

Table 2. Biochemical abnormalities according to age

Characteristic	Age < 6 years n = 27	Age > 6 years n = 69	P
Serum Cholesterol			
Normal, n (%)	23 (85.2 %)	28 (40.6 %)	< 0.001 ¥ HS
High, n (%)	4 (14.8 %)	41 (59.4 %)	
Serum triglyceride			
Normal, n (%)	23 (85.2 %)	31 (44.9 %)	< 0.001 ¥ HS
High, n (%)	4 (14.8 %)	38 (55.1 %)	
Fasting blood sugar			
Normal, n (%)	21 (77.8 %)	20 (29.0 %)	< 0.001 ¥ HS
High, n (%)	6 (22.2 %)	49 (71.0 %)	
Liver enzymes			
Normal, n (%)	26 (96.3 %)	63 (91.3 %)	0.398 ¥ NS
High, n (%)	1 (3.7 %)	6 (8.7 %)	

n: number of cases; ¥: Chi-square test; HS: highly significant at P ≤ 0.01; NS: Not significant at P > 0.05

Table 3. Chronic medical disorders according to age

Characteristic	Age < 6 years n = 27	Age > 6 years n = 69	P
Hypertension			
Positive, n (%)	2 (7.4 %)	27 (39.1 %)	0.002 ¥ HS
Negative, n (%)	25 (92.6 %)	42 (60.9 %)	
Psychological			
Abnormal, n (%)	1 (3.7 %)	19 (27.5 %)	0.010 ¥ HS
Normal, n (%)	26 (96.3 %)	50 (72.5 %)	
Gall bladder disease			
Positive, n (%)	1 (3.7 %)	1 (1.4 %)	1.000 Y
Negative, n (%)	26 (96.3 %)	68 (98.6%)	
Asthma			
Positive, n (%)	8 (29.6 %)	3 (4.3 %)	0.002 Y HS
Negative, n (%)	19 (70.4 %)	66 (95.7 %)	
Sleep apnea			
Positive, n (%)	5 (18.5 %)	45 (65.2 %)	< 0.001 ¥ HS
Negative, n (%)	22 (81.5 %)	24 (34.8 %)	
GERD			
Positive, n (%)	1 (3.7 %)	23 (33.3 %)	0.003 ¥ HS
Negative, n (%)	26 (96.3 %)	46 (66.7 %)	
MS pain			
Positive, n (%)	2 (7.4 %)	14 (20.3 %)	0.223 Y NS
Negative, n (%)	25 (92.6 %)	55 (79.7 %)	
IDA			
Positive, n (%)	26 (96.3 %)	24 (34.8 %)	< 0.001 ¥ HS
Negative, n (%)	1 (3.7 %)	45 (65.2 %)	

n: number of cases; ¥: Chi-square test; Y: Yates correction; HS: highly significant at P ≤ 0.01; NS: Not significant at P > 0.05

Discussion

Childhood obesity is recently considered to be a major growing health problem that has many adverse effects on children health[49].

In this study, the patients involved were classified in to two groups (2-6 years) and (6-18 years), mean age was higher among the older age group which may reflect that the risk of obesity increases with age and it's a real progressing issue that once occur it may increase with time.

This was consistent to a study at Al Basrah city in Iraq where it found that the risk of overweight and obesity increases from 17.8% at 8 years to 30.4% at 11 years old[50]. It's also seen by many other studies[51-57].

By Nablus and Costo Rican study, the prevalence was highest among those 7-9 years old.[58,59]

Gender was not significantly varying between the two age group, which is consistent with 2 studies in Iraq and one Italian study which may reflect that dietary habit among societies and their life style is the determinant rather than gender[50,52,60]. Some studies have shown more male preponderance[58,59,61]; others show female preponderance as a risk factor[56,62,63].

Regarding residency, there is significant correlation between obesity and urban residency among older age group that is consistent with Riyadh et al study in Iraq[52] and Zugue et al in USA[64], Friedrik et al[65], Behrman et al[66] who found that trends were more marked and consistent with urban residency which can be explained by the more marked un healthy life style.

On evaluating the correlation between socioeconomic status and obesity, its more pronounced with good status but no significant difference between the two groups. The parallel correlation was also noted by a study in AL Basrah city[50].

By many other studies, the result was on the reverse[67-69].

By others its seems that in lower income countries, the higher socio -economic status, the more rate of obesity, while in high income countries they are less likely to be obese[70], this may reflect that the low income society high income persons have higher tendency to consume high carbohydrate diet and to have less physical activity, and the opposite for high income society.

Impaired glucose tolerance, dyslipidemia, hypertension, sleep abnormalities were reported more significantly among the older age group as obesity-related adverse health effect that increases with severity and chronicity of obesity[71-74].

Elevated liver enzymes were still reported in both groups with higher percent among older one but no statistical

significance between them. It's still a reported health problem of obese patient by many other studies[75].

Gall bladder stones was also seen in our patient of both groups but it's considered less to be reported among children and adolescents, similarly musculoskeletal pain had no statistical significance, it is a subjective problem that depend on patient pain threshold and severity of obesity rather than age group[76,77].

Only asthma and iron deficiency anemia were found to be significantly seen among the younger one.

Asthma among obese patients is still an increasing problem among obese by 2 fold than non-obese. Being higher in younger age may be related to the higher rate of asthma in general among younger rather than secondary to obesity.[78-81]

Iron deficiency anemia may be a reflective to poor dietary iron intake and impaired iron absorption being more pronounced among younger age group. Its seen that the prevalence of iron deficiency increases as BMI increase[80-83].

Conclusions

Obesity is a real recent health problem among children and adolescents with many negative impacts on their health.

Increasing awareness about the consequence of obesity is crucial in our society.

Social education about prevention methods is the main step in controlling this disease and its consequences.

References

1. Robert M Nalina and Peter T Katzmarzyk. Validity of the body mass index as an indicator of the risk and presence of overweight in adolescents. American Journal of Clinical Nutrition. 1999; 70:131S–136S.
2. Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. BMJ. 2000; 320:1240–1243.
3. Eric Ravussin and Boyd A. Swindurn. Pathophysiology of obesity, Lancet. 1992;340–404.
4. Must A, Strauss RS Risks and consequences of childhood and adolescent obesity. Int J Obes Relat Metab Disord (1999) 23 Suppl 2: S2–11.
5. Pulgaron ER (2013) Childhood obesity: a review of increased risk for physical and psychological comorbidities. Clinical Therapeutics 35(1):A18-32
6. Park MH, Falconer C, Viner RM et al. (2012) The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev 13(11):985-1000.
7. Pietrobelli A, Faith MS, Allison DB, et al. Body mass index as a measure of adiposity among children and adolescents: A validation study. J Pediatr. 1998; 132:204-210.
8. NHANES 2000 CDC Growth Charts: United States. Available at: http://www.cdc.gov/growthcharts/. Accessed on February 8, 2006.
9. Gesellschaft für Versicherungswissenschaft und-gestaltung e.V. (2017) Kooperationsverbund "gesundheitsziele.de". http://gesundheitsziele.de/ (As at 30.01.2017).
10. Kliegman RM, Behrman RE, Jenson HB, Stanton. Nelson's textbook of peadiatrics. Sheila Gahagan Chapter 47 Overweight and Obesity ,20th ed. 2016 p;307-316.
11. Koplan JP, Liverman CT, Kraak V, eds. Preventing Childhood Obesity: Health in the Balance. Washington, DC: National Academic Press, 2005.
12. Han JC, Kimm SYS. Childhood Obesity-2010: Progress and Challenges. Lancet 2010; 375:1737-1748.
13. Lustig RH and Weiss R. Disorders of energy balance. In: Sperling MA (ed) Pediatric Endocrinology (third edition). Saunders Elsevier, Philadelphia, PA 2008:788-838.
14. Center for Disease Control and Prevention. Contributing factors. Available from: http://www.cdc.gov//obesity/ childhood/ contributing factors,2010. html [Last accessed on 2014 Jul 01].
15. Davison KK, Birch LL. Childhood overweight: A contextual model and recommendations for future research. Obes Rev 2001; 2:159-71.
16. Anderson PM, Butcher KE. Childhood obesity: Trends and potential causes. Future Child 2006;16:19-45.
17. Kapil U, Bhadoria AS. Television viewing and overweight and obesity amongst children. Biomed J 2014;37:337-8. Available from: http://biomedj.org/preprintarticle. 125654 [Last accessed on 2014 Jul 11].
18. Weinstein LS, Chen M, Liu J. Gsa<(alpha) mutations and imprinting defects in human disease. Ann NY Acad Sci 2002;968:173-197.
19. Ong KK, Loos RJ. Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. Acta Paediatr 2006;95: 904-908.
20. Owen CG, Martin RM, Whincup PH, Smith GD, Cook DG. Effect of infant feeding on the risk of obesity across the life course: a quantitative review of published evidence. Pediatrics 2005; 115: 1367-1377.
21. Chhatwal J, Verma M, Riar SK. Obesity among pre-adolescent and adolescents of a developing country (India). Asia Pac J Clin Nutr 2004; 13:231-5
22. Freedman DS, Khan LK, Serdula MK, Ogden CL, Dietz WH. Racial and ethnic differences in secular trends for childhood BMI, weight, and height. Obesity (Silver Spring) 2006; 14:301- 308.
23. Yajnik CS, Lubree HG, Rege SS, Naik SS, Deshpande JA, Deshpande SS, Joglekar CV, Yudkin JS. Adiposity and hyperinsulinemia in Indians are present at birth. J Clin Endocrinol Metab 2002; 87:5575-5580.
24. Hubbard VS. Defining overweight and obesity: what are the issues? Am J Clin Nutr 2000; 72:1067-1068.
25. Gupta RK. Nutrition and the Diseases of Lifestyle. In: Bhalwar RJ, editor. Text Book of Public health and Community Medicine. 1st ed. Pune: Department of community medicine. AFMC, New Delhi: Pune in Collaboration with WHO India Office; 2009. p. 1199.
26. Laxmaiah A, Nagalla B, Vijayaraghavan K, Nair M. Factors affecting prevalence of overweight among 12 to 17 year old urban adolescents in Hyderabad, India. Obesity (Silver Spring) 2007;15:1384-90.

27. Chhatwal J, Verma M, Riar SK. Obesity among pre-adolescent and adolescents of a developing country (India). Asia Pac J Clin Nutr 2004; 13:231-5.

28. Panjikkaran ST, Kumari K. Augmenting BMI and Waist-Height Ratio for establishing more efficient obesity percentiles among school children. Indian J Community Med 2009; 34:135-9.

29. Atkinson RL, Dhurandhar NV, Allison DB, Bowen RL, Israel BA, Albu JB, Augustus AS. Human adenovirus-36 is associated with increased body weight and paradoxical reduction of serum lipids. Int J Obes (Lond) 2005; 29:281-286.

30. Goldfield GS, Moore C, Henderson K, Buchholz A, Obeid N, Flament MF. Body dissatisfaction, dietary restraint, depression, and weight status in adolescents. J Sch Health 2010;80:186-92.

31. American Academy of Pediatrics. About childhood obesity. Available from: http://www.aap.org/obesity/about. html [Last accessed 2014 Jul 14].

32. Niehoff V. Childhood obesity: A call to action. Bariatric Nursing and Surgical Patient. Care 2009; 4:17-23.

33. Srinivasan SR, Bao W, Wattigney WA, Berenson GS. Adolescent overweight is associated with adult overweight and related multiple cardiovascular risk factors: The Bogalusa Heart Study. Metabolism 1996; 45:235-240.

34. Section on Pediatric Pulmonology, Subcommittee on Obstructive Sleep Apnea Syndrome. American Academy of Pediatrics. Clinical practice guideline: diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2002; 109:704-712.

35. Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. JAMA 2004;291:2013-2016.

36. Wiegand S, Maikowski U, Blankenstein O, Biebermann H,Tarnow P, Gruters A. Type 2 diabetes and impaired glucose tolerance in European children and adolescents with obesity – a problem that is no longer restricted to minority groups. Eur J Endocrinol 2004;151:199-206.

37. Klish WJ. Clinical evaluation of the obese child and adolescent.In: Motil KJ, Geffner M (section eds) and Hoppin AG (Deputy ed). Up to date. www.uptodate.comc2013UpTo Date.6. BMI curves. http://www.cdc.gov /growth charts.

38. Huang JS, Barlow SE, Quiros-Tejeira RE, Scheimann A, Skelton J, Suskind D, Tsai P, Uko V, Warolin JP, Xanthakos SA; The NASPGHAN Obesity Task Force. Consensus Statement: Childhood Obesity for Pediatric Gastroenterologists. J Pediatr Gastroenterol Nutr 2013;56:99-109.

39. Lavine JE1, Schwimmer JB, Van Natta ML et al, Nonalcoholic Steato hepatitis Clinical Research Network. Effect of vitamin E or metformin for treatment of nonalcoholic fatty liver disease in children and adolescents: the TONIC randomized controlled trial. JAMA 2011;305:1659-1668.

40. Neslihan Koyuncuo◄u Gungor, Overweight and Obesity in Children and Adolescents J Clin Res Pediatr Endocrinol 2014;6(3):129-143

41. Wald AB, Uli NK. Pharmacotherapy in pediatric obesity: current agents and future directions. Rev Endocr Metab Disord 2009;10:205-214.

42. Farooqi IS, Jebb SA, Langmack G, Lawrence E, Cheetham CH, Prentice AM, Hughes IA, McCamish MA, O'Rahilly S. Effects of recombinant leptin therapy in a child with congenital leptin deficiency. N Engl J Med 1999;341: 879-884.

43. Lustig RH and Weiss R. Disorders of energy balance. In: Sperling MA (ed) Pediatric Endocrinology (third edition). Saunders Elsevier, Philadelphia, PA 2008:788-838.

44. Lustig RH, Hinds PS, Ringwald-Smith K, Christensen RK, Kaste SC, Schreiber RE, Rai SN, Lensing SY, Wu S, Xiong X. Octreotide therapy of pediatric hypothalamic obesity: a double-blind, placebo-controlled trial. J Clin Endocrinol Metab 2003;88: 2586-2592.

45. Nicolai JP, Lupiani JH, Wolf A J. An Integrative approach to obesity. In: Rakel D (ed). Integrative Medicine (3rd ed). W.B. Saunders (Elsevier), Philadelphia, PA 2012:364-375.

46. Crocker MK, Yanovski JA. Pediatric obesity: Etiology and treatment. Endocrinol Metab Clin North Am 2009; 38:525-548.

47. Pulgaron ER (2013) Childhood obesity: a review of increased risk for physical and psychological comorbidities. Clinical Therapeutics 35(1): A18-32.

48. Mayyada Abd-el-Jaleel Salman, Narjis A. H. Ajeel, Prevalence of Overweight and Obesity among Public Primary School Children in Basrah City, iraqi J. Comm. Med., Apr. 2013 (2), p: 103-108.

49. Kliegman RM, Behrman RE, Jenson HB, Stanton. Nelson's textbook of peadiatrics. 18th ed. Philadelphia: W.B. Sanders Company; 2007.p. 232-242.

50. Riyadh K. Lafta, Maher J. Kadhim Childhood obesity in Iraq: prevalence and possible risk factors Ann Saudi Med 25(3) May-June 2005; p:389-393

51. Magarey AM, Daniels LA, Boulton TJ, Cockington RA. Predicting obesity in early adulthood from childhood and parental obesity. International Journal of Obesity 2003; 27:505–513.

52. Kinra S, Nelder RP, Lewendon GJ. Deprivation and childhood obesity: a cross sectional study of 20 973 children in Plymouth, United Kingdom. J Epidemiol Community Health 2000; 54:456–460.

53. Al-Sharif MSA. Risk Factors Associated with Obesity in Children age 6-12 years in Nutritional Clinic at Security Forces Hospital in Riyadh City. MSc. thesis, King Saud University; 2008.

54. Khader Y, Irshaidat O, Khasawneh M, Amarin Z, Alomari M, Batieha A. Overweight and Obesity Among School Children in Jordan: Prevalence and Associated Factors. Maternl Child Health Journal 2009; 13(3):424-431.

55. Langnase K, Mast M, Muller MJ. Social class differences in overweight of prepubertal children in northwest Germany. Int. J Obese Relat Metab Disord 2002; 26: 566–572.

56. Isbaih MA. Prevalence of Overweight and Obesity among School-Age Children in Nablus City. MSc thesis, An-Najah National University, Nablus, Palestine; 2009.

57. Núñez-Rivas HP, Monge-Rojas R, L eón H, Roselló M. Prevalence of overweight and obesity among Costa Rican elementary school children. Rev Panam Salud Publica/Pan Am J Public Health 2003; 13(1):24-32.

58. Bertoncello C, Cazzaro R, Ferraresso A, Mazzer R, Moretti G. Prevalence of overweight and obesity among school-aged children in urban, rural and mountain areas of the Veneto Region, Italy. Public Health Nutrition 2007; 11(9): 887–890.

59. Hedley A, Ogden C, Johnson C, Carroll M, Curtin L, Flegal K. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. JAMA 2004; 29(23):2847-2850.

60. El-Bayoumy I, Shady I, Lotfy H. Prevalence of obesity among adolescents (10 to 14 years) in Kuwait. Asia Pac J Public Health 2009; 21(2):153-159.

61. Qotba H, Al-Isa AN. Anthropometric measurements and dietary habits of school children in Qatar. Int J Food Sci Nutr 2007; 58(1):1-5.

62. Zuguo Mei, Kelly S Scanlon, Laurence M Grummer-Strawn, David S Freedman, Ray Yip and Frederick L Trowbridge. Increasing prevalence of overweight among US low-income preschool children: The center for disease control and prevention pediatric nutrition surveillance, 1983 to 1995.Pediatric. 1998;101: e 12.

63. Fredriks AM, van Buuren S, Burgmeijer RJF, et al. Continuing positive secular growth changes in the Netherlands 1955–1997. Pediatr Res. 2000 [In press].

64. Behrman RE, Kliegman RM, Jenson HB. Nelson textbook of pediatrics, 2000. W.B Saunders company. Chap 16, Obesity;172–176.

65. WHO. Obesity: Preventing and managing the global epidemic. Geneva: WHO Technical report series 894; 2000.

66. Wang Y, Beydoun MA. The Obesity Epidemic in the United States—Gender, Age, Socioeconomic, Racial/Ethnic, and Geographic Characteristics: A Systematic Review and Meta-Regression Analysis. Epidemiol Rev 2007; 29:6–28.

67. Truswell AS. Overweight and obesity. In: ABC of Nutrition. 4th ed. London: BMJ Publishing Group; 2003.p.69-77.

68. A.K. Ravishankar, "Is India Shouldering a Double Burden of Malnutrition?" Journal of Health Management 14, no. 3 (2012): 313-28.

69. Gesellschaft für Versicherungswissenschaft und -gestaltung e.V. (GVG) (2017) Kooperationsverbund "gesundheitsziele.de". http://gesundheitsziele .de/ (As at 30.01.2017)

70. Medizinischer Dienst des Spitzenverbandes Bund der Krankenkassen e.V. (MDS), GKV-Spitzenverband (GKV) (2015) Präventionsbericht 2015 - Leistungen der gesetzlichen Krankenversicherung: Primärprävention und betriebliche Gesundheitsförderung - Berichtsjahr 2014.

71. Rao M, Afshin A, Singh G et al. (2013) Do healthier foods and diet patterns cost more than less healthy options? A systematic review and meta-analysis. BMJ Open 3(12):e004277.

72. Moss A, Klenk J, Simon K et al. (2012) Declining prevalence rates for overweight and obesity in German children starting school. European Journal of Pediatrics 171(2):289-299.

73. Statistisches Bundesamt (2016) Land- und Forstwirtschaft, Fischerei: Bodenfläche nach Art der tatsächlichen Nutzung. Fachserie 3 Reihe 51. Destatis, Wiesbaden.

74. Holcomb GW Jr, Holcomb GW 3rd. Cholelithiasis in infants, children, and adolescents. Pediatr Rev 1990; 11:268–274.

75. Miltenburg DM, Schaffer R 3rd, Breslin T, et al. Changing indications for pediatric cholecystectomy. Pediatrics 2000; 105:1250–1253.

76. Chen Y.C., Dong G.H, Lin K.C., Gender difference of childhood overweight and obesity in predicting the risk of incident asthma. A systematic review and meta-analysis. Obes.rev.2012;14;222-231.

77. Jason E. Lang, M.D, Obesity, Nutrition, and Asthma in Children, Pediatr Allergy Immunol Pulmonol. 2012 Jun; 25(2): 64–75.

78. Karen G, Halterman J, Kaczorowski JM et al, overweight children and adolescent; a risk group for iron deficiency anemia. Pediatrics.2004;14;104-8.

79. Qasim MT, Al-Mayali HK. Investigate the relation between Baicalin effect and Gene expression of LH, FSH, Testosterone in male rats treated with Gemcitabine drug. Research Journal of Pharmacy and Technology. 2019 Sep 30;12(9):4135-41.

80. Qasim MT, Al-Mayali HK. The immunological and protective role of Baicalin in male rats treated with chemotherapy (Gemcitabine). In-Journal of Physics: Conference Series 2019 Jul 1 (Vol. 1234, No. 1, p. 012065). IOP Publishing.

81. Tahmasebi S, Qasim MT, Krivenkova MV, Zekiy AO, Thangavelu L, Aravindhan S, Izadi M, Jadidi‐Niaragh F, Ghaebi M, Aslani S, Aghebati‐Maleki L. The effects of Oxygen‐Ozone therapy on regulatory T‐cell responses in multiple sclerosis patients. Cell biology international. 2021 Mar 16.

82. Mousa HM, Qasim MT. Microbial Infection and IL-6 Urine Levels for Pregnant women in Thi-Qar Province. World J. Pharma. Res. 2015 Mar 6;4(05):358-65.

83. Ahmed Jassem AL-Naely, Maytham T. Qasim, Hussein Abbas Al-Hamadawi. Transfusion of Blood Components in the Newborn Service of the Hospital. Annals of RSCB [Internet]. 2021Apr.7 [cited 2021Apr.14];952-8. Available from: http://annalsofrscb.ro/index.php/journal/article/view/2525.

84. Zainab I. Mohammed, Maytham T. Qasim. Correlation of AMH and LH Levels in PCOS Patients with Pregnancy Rate. Annals of RSCB [Internet]. 2021Apr.7 [cited 2021Apr.14];:945-51. Available from: http://annalsofrscb.ro/index.php/journal/article/view/2524.