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A Review on Higher BMI In Children Future Predictive for Metabolic Syndrome: Targeting Obesity Associated Consequences

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Abstract

Obesity among children in the U.S. and across the world is a significant problem for public health, yet very less is documented about the health effects of pre-teen and/or child obesity. Adiposity in children has been viewed as a potential risk to community health since it has been shown to be a predictor of chronic illness, which is becoming more frequent at a younger age. Although the waist circumference (WC) in the child community is not a standard assessment in the clinical settings, numerous studies have proven the fact that in children and adolescents, WC is a predictor for cardio-metabolic health. In a cross-sectional assessment that included several regression models, WC explained a higher fraction of variation in key variables for cardiovascular disease than BMI. The results of different studies comparing body mass index (BMI) to WC have been inconsistent. While combining BMI and WC did not strengthen prediction over either BMI or WC alone, in stratified analysis, high WC was observed to increase the likelihood of coronary artery disease among BMI subgroups. Moreover, the BMI and WC are significantly linked, their value in screening children at risk for metabolic syndrome (MetS) is still controversial. In this study we are thus examining the prognostic likelihoods of BMI, WC and their combinations with children MetS.

Keywords: Body Mass Index, Visceral Adiposity, WC, MetS

Introduction

The MetS is a term that most doctors and health professionals have heard or read about. For example, as of July 2021, a PubMed search for "metabolic syndrome" returned almost 389077 papers since Grundy and colleagues introduced the idea in 2001[1]. Although many medical practitioners are familiar with the NCEP-ATP III's five diagnostic criteria (abnormal lipid profiles, specifically hypertension, impaired glucose tolerance, reduced HDL cholesterol and central obesity or WC), variables used and the rationale for establishing cut-offs remain obscure to many people. Additionally, a description of MetS based on conceptual definitions is sometimes confounded with the diagnostic methods (the five necessary elements) that have been presented[2, 3].

In America and across the globe, obesity in children is a significant community health problem, but much less is documented on the health implications of prenatal and/or childhood obesity. In most High income nations as well as in several countries of low and medium income, childhood overweight and obesity increased throughout the 1980s as well as 1990s to present days. In the U.S., about 17% of children aged 2 to 19 are overweight, while another 16% are at risk of overweight [4, 5]. Children's obesity is becoming an issue of public health as chronic illnesses including stroke, CVD, hypertension, diabetes, osteoarthritis, several malignant diseases are likely to be predictive and increasingly common at an even earlier age [6, 7]. Childhood obesity increases concern that the total morbidity and death will start earlier than expected in adulthood [8]. This metabolic dysregulation is facilitated by complicated interactions between an unhealthy or insufficient food, insufficient physical exercise or a sedentary lifestyle, and genetic predisposition[9, 10]. In children under the age of five the prevalence of weight gain as well as obesity is usually increasing. Childhood obesity and overweight persist throughout adulthood, which means that patterns in early childhood give insight into future disease incidence. Recognizing young children with raised MSRF characteristics is becoming a public health and clinical priority, as it is achievable that appropriate strategies aimed at reducing cardiovascular risk can be implemented more successfully in

children than it is to modify behaviours later in life after detrimental health practises have become developed[11]. There is no consensus on what this level should be, and it is evident that both the overall percentage of body fat and the associated health hazards vary by sex, age, and a variety of other variables and are not constant between BMI categories. Overall, age and sex adjusted BMIs were utilised to identify child obesity since the weight and height scales and easily available universal growth charts may be achieved with relative simplicity. Additionally, because waist circumference (WC) is a measurement for visceral fat, a kind of adipose tissue that has been linked with a greater risk of metabolic illness, individuals with a higher level of visceral fat are at a greater risk of metabolic disease [12]. The results of several research compared BMI to WC were conflicting. Nevertheless, Janssen et al. [13] released a paper that exhibits While combining BMI and WC did not strengthen prediction over either BMI or WC alone, in stratified analysis, high WC was observed to increase the likelihood of coronary artery disease among BMI subgroups. Another research study in Jansse et al found that the projected chance of adult MetS in BMIs in children between the 50th and 84th percentiles and between the 85th and 94th percentiles rose with WC — notably around the 90th percentile mark. In addition, the scientific enhancement has proven the usefulness of WC for preventing metabolic diseases in children with normal weights. Several studies have indicated that WC is an independent predictor of an abnormal lipid profile, hypertension, and insulin resistance[14-17]. Although the WC in the child community is not a standard assessment in the clinical settings, numerous studies have proven the fact that in children and adolescents, WC is an excellent predictor for CVD risk factors. In-addition, several findings consistent with above research. Savva et al. [18] found that WC in cross-sectional study employing multiple regression analysis explains a larger percentage of cardiovascular variability risk factors than BMI. Additionally, Sellers et al.[19] reported that WC was linked with insulin resistance more strongly than BMI in a dataset of Australian Aboriginal children. Moreno et al. [20] found that, in spite of a statistically significant difference in AUC between BMI and WC, WC appears to be the best anthropometric screening technique in children for MetS. Naturally, this variation is due to changes in study design, demographic characteristics, anthropometric indices, WC measurement location, and statistical methodology. However, the BMI and WC are significantly linked, their value in screening children at risk for metabolic syndrome is still controversial. In this study we are thus examining the prognostic likelihoods of BMI, WC and their combinations with children MetS.

Selection of literature review

Articles were retrieved by manual screening of relevant reference lists in Pub Med, Cochrane, ScienceDirect, Embase, and Springer. While multiple keywords were used in addition to the literature review, including BMI Range in Children, Epidemiology of Childhood MetS, Pathophysiology of MetS in Association with Central Obesity, Relationship between central obesity or waist circumference and metabolic syndrome, and Association between higher BMFI predictive for metabolic syndrome, this article. Additionally, reference lists are checked for papers that were not included in the first search.

MetS pathophysiology in relation to BMI and central obesity models

In adults the BMI is defined as being overweight in 25.0–29.9 kg/m2 and the BMI as being obese in 30 kg/m2 or higher[21]. A higher BMI was recognised by updated epidemiological studies as a risk factor to a growing spectrum of chronic diseases [22]. Additionally, for every five units rise in BMI above 25 kg/m2, total death increases by 29 percent, vascular mortality increases by 41 percent, and diabetes-related mortality increases by 210 percent[23]. The cardiometabolism risk forecast, which is not immediately determinable by high BMI, is calculated by measurements of central or abdominal adiposity such as the increased WC[24, 25]. However, emerging researches has established a link between childhood adiposity and the eventual development of a cluster of cardiometabolic risk indicators defined by reduced insulin sensitivity, hyperlipidemia, and high blood pressure, popularly known the cardiometabolic syndrome[26], syndrome X[27], metabolic syndrome[28] and plurimetabolic syndrome[29] (Figure 1).

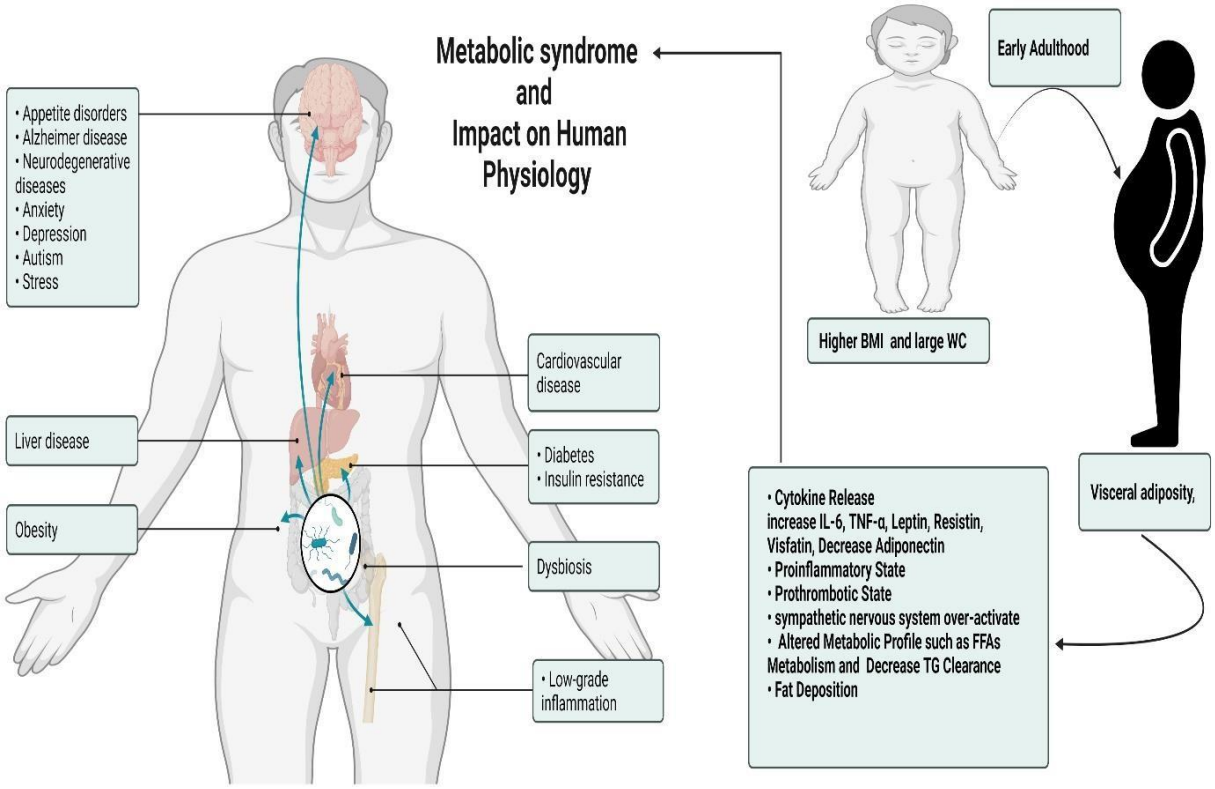

Figure 1: Demonstrate the pathophysiology of metabolic syndrome and its impact on human physiology in early adulthood years

The visceral fat, which shows its unique pathphysiologic function, is obviously connected to insulin resistance rather than general obesity. Adiposity in the abdomen, as assessed by WC, has been identified as a risk factor for stroke, CVD, hypertension, and insulin resistance [30-32]. However, there are conflicting processes which have the especially detrimental consequences of visceral fat. While rodent models were very beneficial since we were able to modify rat genetics, they do have certain disadvantages. Longitudinal studies are complicated, physiological evaluation techniques are sophisticated, and rat obesity may be a poor predictor for intermediate human obesity, which contributes for the majority of the prevalent population threat. Although rodent recovery increases insulin action [33], there is a 1:1 relationship between fat accumulation in rats and humans, which makes it difficult to comprehend. Primate models could be more interesting and informative, but interventional studies are hard and expensive; research in human intervention are even more complex.

Adipocytes are now seen to be endocrine cells, which release certain substances into the circulation. Although most of these substances are not characterised, others undoubtedly are cytokines, such as IL-6, TNF-α and resistin, leptin, adiponectin and visfatin. It is interesting to notice that the insulin sensitivity in liver and muscles is determined by these molecules, which might therefore be "bad actors" within the context of the metabolic syndrome. An increase in cytokines or inadequate decrease of adiponectin release cannot be ruled out as significant contributors for the insulin resistance progression to fat. Alternate possibilities include the likely role of the FFAs. According to Arner and his collaborators[34], the release of FFAs from visceral fat into the portal vein, which travels directly to the liver, may have a negative influence on the insulin activities of FFAs (portal theory). Increasing FFAs are reported to lead to significant insulin resistance within a few of hours by infusion of a lipid emulsion[35, 36]. Griffin and colleagues[37] investigated the effect of this treatment and believed that FFAs interfere with insulin signalling through a serine kinase cascade mediated by protein kinase C, leading in dysfunctional insulin sensing and glucose

uptake. Ellmerer and collaborators [38] showed that insulin is significantly hampered by its capability to promote macromolecular dispersions in the fat-fed obese dog model as well as by its own access to the skeletal muscles. This phenomenon has been replicated in a preliminary manner using lipid infusion. As a result, The FFAs are thus strong players for mediating the effects of fat accumulation leading to insulin resistance. Interestingly, after many investigations of fat-induced resistance to insulin, we found no significant alterations in adipokine gene expression in abdominal or hepatic fat. However, we detected a coordinated rise in the expression of gluconeogenic genes in the hepatocytes (fatty acid–binding protein, PEPCK, glucose-6 phosphatases, CPT1), FFA-induced genes upregulation of the abdominal fat accumulation (PPAR–γ, hormone-sensitive lipase, SREBP-1 transcription factor) [39]. Additionally, the sympathetic nervous system (SNS) may enhance FFA flow to the hepatocytes and other organs sensitive to insulin. Researchers also found the effect of insulin on FFA and glycerol, along with the variation in arteriovenous effects across the abdominal fat depot. Moreover, lipolytic burst, with the β3 blocking drug bupranolol, was entirely suppressible (the dog's β3-adrenergic main receptors to the visceral fat depot are located)[40]. Hsu and his colleagues [41]have also discovered in the preliminary investigations that time-dependent alteration of FFA are more insulin resistant to liver than continuous hyperlipidemia. Landsberg and colleagues[42] uncovered scientific proof that SNS is active in higher BMI condition and this might play a role in hypertension aetiology. SNS activation in obesity together with the pulsatory release of FFA from the fat depot of the viscera might potentially enhance FFA release into the portal circulation and worsen the liver and skeletal muscle resistance to insulins. Additionally, physiologic alterations such as decreased insulin sensitivity and a gradual rise in beta-cell sensitivity to glucose along with decreased insulin clearance that results in insulin resistance are produced by a small increase in fat consumption in a central obesity model.

Relationship of central obesity or waist circumference with metabolic syndrome

WC has been found in several studies to be a predictor of aberrant lipid levels, hypertension, and insulin resistance, regardless of BMI. In contrast, the development of adult MetS is predicted using measurements of over-obesity (BMI), Kg/m2, and insulin-resistance (IR) in childhood. Thus, these findings from the research comparing BMI to WC have been conflicting. BMI is used to determine the nutritional state and is not an accurate indication for adiposity since the body's fat and lean mass cannot be determined. A recent study discovered that changes in BMI were more closely connected to changes in body fat than changes in WC[43]. However, metabolic Syndrome prevalence is greater in obese children/adolescents than in normal weight[44, 45]. Visceral obesity has been proposed as a potential co-risk factor, owing to its harmful effects in animal models and the substantial epidemiologic evidence implicating it in metabolic dysfunction[46]. Additionally, family connections appear to have an impact on the onset and progression of the MetS. For example, increasing WC in mothers is related with a higher risk of MetS in their future children [47]. Additionally, it has been found that MetS is linked with an increased incidence of CVD, as well as stroke, renal failure, and diabetes, to result in end-organ failure [48]. It appears that the prevalence of MetS has increased over the past two decades, at the same time as the increasing prevalence of obesity among this age group [49]. In this Context, it is noteworthy to highlight that MetS 's prevalence remains virtually unaltered over the last decade, using the same defining criteria, comparable to our earlier observation[50]. As we have seen before both in paediatric age, we discovered a greater prevalency of MetS in male than female[51] (Figure 2).

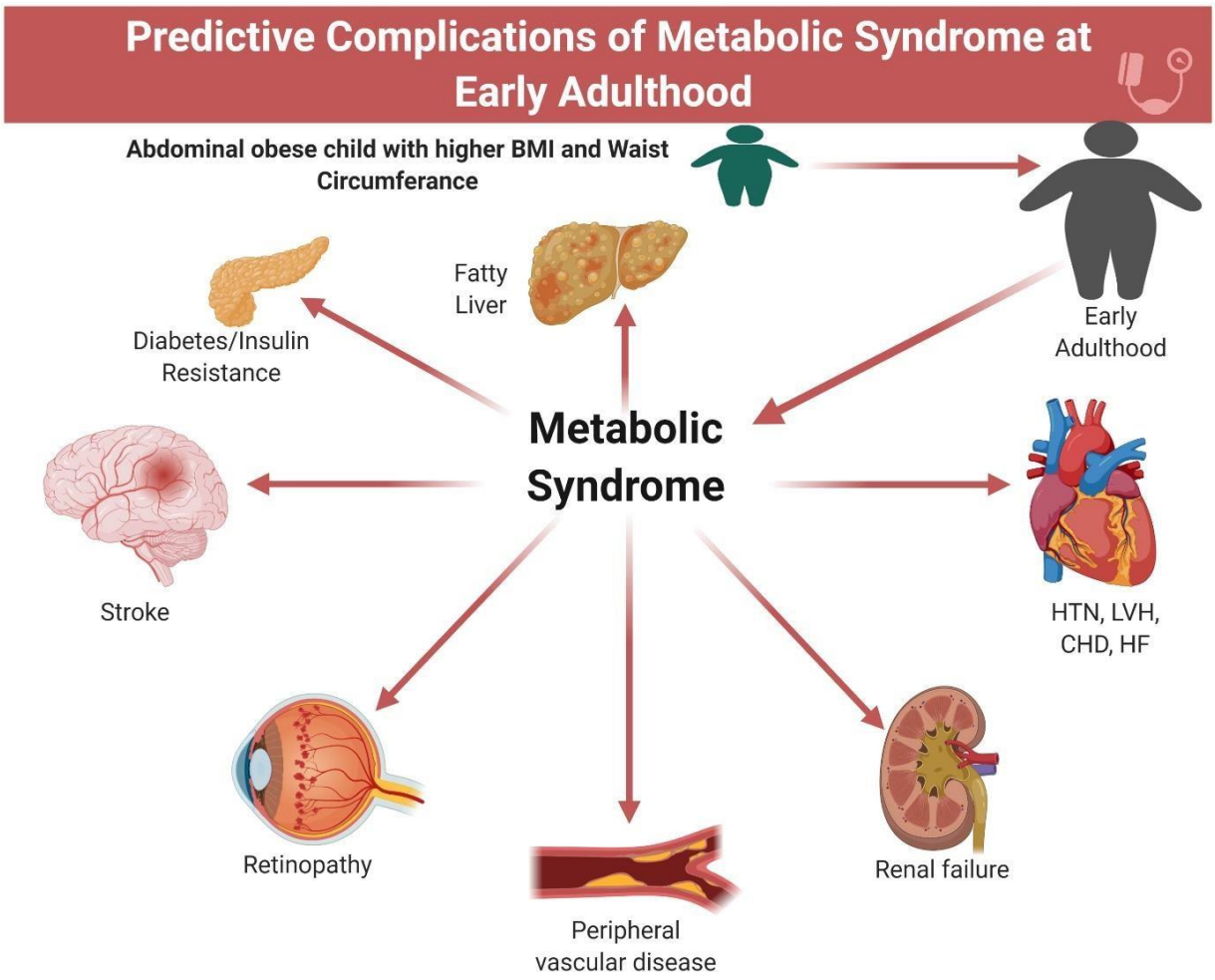

Figure 2: Demonstrate the relationship of higher BMI and waist circumference in children with central adiposity and predictive complication of metabolic syndrome in early adulthood

However, it has been apparent over the past several years that we don't need a count that only predicts excess weight, but that we need a count to indicate if an obese patient already has a cardiometabolic risk. Actually, the index was usually taken as a tool to measure excess weight. The idea that BMI alone cannot adequately describe the risk has resulted in an increased focus on other elements of obesity-related cardiometabolic illness[52]. Due to its pathogénic impact in animal models and its considerable epidemiologic data, Visceral obesity was recommended as a supplementary risk factor in metabolic syndrome[46, 53]. Considering the problems of the BMI, which exclusively determines an over-weight of the patient by height, other indexes were developed which also consider the composition of the body, body fat and the distribution of fat [17]. This study examines the connection between two novel metrics, the body mass fat index (BMFI) and the waist circumference (WC), which was previously considered a very accurate Mets signal in addition to body composition. In obese animal models, malfunctioning visceral adipocytes act as a source of inflammation and insulin resistance [54, 55]. Indeed, the decreased sensitivity to insulin is linked with an greater in human central adiposity[56], and inflammatory condition of abdominal adipose tissues is implicated in the pathogenesis insulin resistance, inflammation, and endothelial dysfunction, among other variables [57]. Several large cohorts in the community demonstrate a link between cardiac metabolism and visceral fat[58], left ventricular remodelling[59], and dysglycemia. The bulk of significant studies carried out in the community showed that visceral adiposity, metabolic

disease and cardiovascular consequences were linked between obese persons and others (e.g., African Americans)[60-63]. Although the Bogalusa Heart Study was initiated before Kalkhoff and team [64, 65] established central adiposity as a diabetes-related determinant and other metabolic disorders, scientists at Bogalusa showed that persistently high insulin[66] and overweight are linked to higher Mets levels, as measured by BMI, later in life instead of WC [67].

The relationship between a higher Body Mass Fat Index (BMFI) and predictive metabolic syndrome

Although BMI is an excellent predictor of body fat[68, 69]. WC is frequently used to assess abdominal adiposity deposition, and comparisons to gold standard methods reveal a high correlation between WC and abdominal adipose tissue. There is controversy in choosing the most precise anthropometric index for MetS predictions in children. BMI is used to determine dietary status and it is not an accurate adiposity indicator, since the body fat is not differentiated from the lean mass. According to a recent study, alterations in BMI are more closely connected to changes in body fat than changes in waist circumference[70]. Some researchers have shown that BMI provides an insight into CVD risk factors in children[71, 72]. A study in Wiley publication revealed that in 6 to 12 years old children MetS was 10.7 percent higher in males than in girls after an average of 6.6 years of follow-up. The prevalence of MetS in the baseline was 9.8 percent, without gender. The increasing prevalence and incidence of MetS in BMI and WC were related with this rise. The optimum BMI cut-off values for predicting MetS in children aged 6–12 years were 16.5 kg/m2 for boys and 16.3 kg/m2 for girls, and 57.5 cm for boys and 56.5 cm for girls[73]. Some studies have shown that central obesity is linked to an increasing risk of MetS. Sun & coauthor [74] showed that children with BMI or WC higher than specified threshold had a high risk of development of adult MetS in longitudinal investigation. Farin and co-workers[75] found, increasing obesity deteriorated insulin sensitivity and associated cardio-metabolic risk variables, independent of whether BMI or waist circumference was employed to measure excess adiposity. Furthermore, a national CASPIAN survey in Iran reveals that the percentage of the CVD risk factors and MetS in children with combined obesity was dramatically higher than the number of children of the isolated types of obesity[76], evidence which are consistent, indicating that both BMI and WC have a critical role in MetS. It is controversial that the anthropometric action is more appropriate for the MetS prognosis of the kid. The same predictability for MetS exists for both BMI and WC in this study. Among a cohort research, Garnett and colleagues[77], showed that BMI is an established metric for identifying children at greater risk of CVD risk factors in adolescents who do not have to assess WC in combination to BMI. BMI has demonstrated the greatest predictive ability to identify MetS in a further cross-sectional study[18, 78]. A research finding demonstrate the clinical explanation by indicating that the normal BMI group had the lowest diastolic and systolic blood pressures while the other BMI groups had the highest. Plasma insulin and CRP levels also rose considerably when BMI increased. The existing clinical tools of BMI and waist circumference to evaluate obesity risks were strongly linked to visceral fat and the weight changes were minor compared to the accompanying changes in visceral or subcutaneous fat. Finally, incident MetS was substantially linked to visceral fat (both at one single moment and its change over time). These data imply that, even in people with MetS, when BMFI increases, the risk of dyslipidemia, hypertension, and inflammation increases[79] (Figure 3).

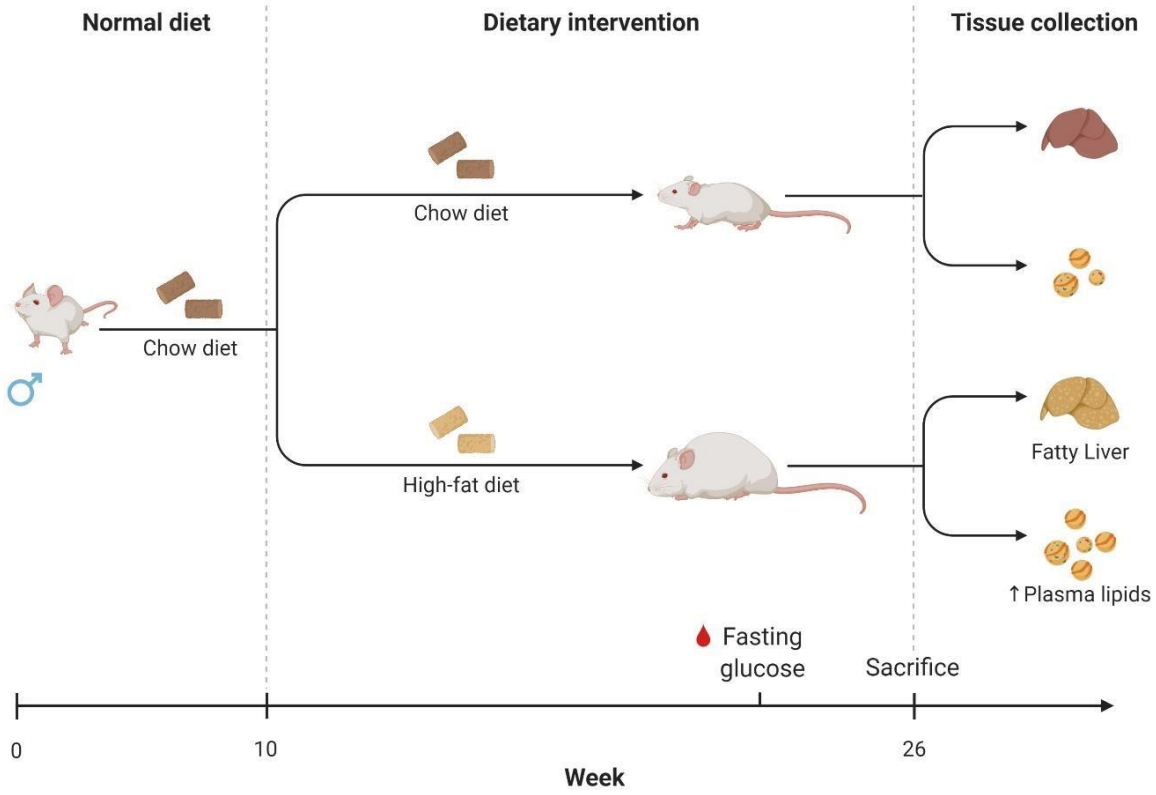

Figure 3: Demonstrate the high fat diet experimental timeline animal model and change in biochemical parameters

Conclusion

In summary, both BMI and WC are able to predict MetS and children with a little bigger BMI or WC which are substantially more vulnerable to MetS. Notably, the severity of MetS with BMI predicts future illness and the measurement using WC. The BMI trend in both boys and girls is varied; BMI cut-off values have thus been modified for sex and age. Future investigations might determine if there are various variables for prediction of MetS in gender and in different ages with varying predictive abilities. Furthermore, the high prevalence of MetS in children in the short follow-up period shows the need of early childhood intervention efforts. Therefore, primary prevention in late adolescent and young adulthood metabolic syndrome development may start with attempts at reducing BMR, WC or early childhood adiposity associated insulin resistance.

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References:

1. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III), Jama, 285 (2001) 2486-2497.
2. J.P. Després, I. Lemieux, J. Bergeron, P. Pibarot, P. Mathieu, E. Larose, J. Rodés-Cabau, O.F.

Bertrand, P. Poirier, Abdominal obesity and the metabolic syndrome: contribution to global cardiometabolic risk, Arteriosclerosis, thrombosis, and vascular biology, 28 (2008) 1039-1049.
3. J.P. Després, I. Lemieux, Abdominal obesity and metabolic syndrome, Nature, 444 (2006) 881-887.
4. C.L. Ogden, M.D. Carroll, L.R. Curtin, M.A. McDowell, C.J. Tabak, K.M. Flegal, Prevalence of overweight and obesity in the United States, 1999-2004, Jama, 295 (2006) 1549-1555.
5. J.P. Koplan, C.T. Liverman, V.I. Kraak, Preventing childhood obesity: Health in the balance: Executive summary, Journal of the American Dietetic Association, 105 (2005) 131-138.
6. P.A. Tataranni, C. Bogardus, Changing Habits to Delay Diabetes, New England Journal of Medicine, 344 (2001) 1390-1392.
7. D.F. Williamson, The Prevention of Obesity, New England Journal of Medicine, 341 (1999) 1140-1141.
8. J.A. Morrison, L.A. Friedman, C. Gray-McGuire, Metabolic Syndrome in Childhood Predicts Adult Cardiovascular Disease 25 Years Later: The Princeton Lipid Research Clinics Follow-up Study, Pediatrics, 120 (2007) 340-345.
9. R.M. Leech, S.A. McNaughton, A. Timperio, The clustering of diet, physical activity and sedentary behavior in children and adolescents: a review, International Journal of Behavioral Nutrition and Physical Activity, 11 (2014) 4.
10. A. Marti, M.A. Martinez-González, J.A. Martinez, Interaction between genes and lifestyle factors on obesity: Nutrition Society Silver Medal Lecture, Proceedings of the Nutrition Society, 67 (2008) 1-8.
11. R. Kahn, J. Buse, E. Ferrannini, M. Stern, The Metabolic Syndrome: Time for a Critical Appraisal, Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes, 28 (2005) 2289-2304.
12. P. Calabro, E.T.H. Yeh, Intra-abdominal adiposity, inflammation, and cardiovascular risk: New insight into global cardiometabolic risk, Current Hypertension Reports, 10 (2008) 32-38.
13. I. Janssen, P.T. Katzmarzyk, S.R. Srinivasan, W. Chen, R.M. Malina, C. Bouchard, G.S. Berenson, Combined Influence of Body Mass Index and Waist Circumference on Coronary Artery Disease Risk Factors Among Children and Adolescents, Pediatrics, 115 (2005) 1623-1630.
14. S. Lee, F. Bacha, S.A. Arslanian, Waist circumference, blood pressure, and lipid components of the metabolic syndrome, The Journal of Pediatrics, 149 (2006) 809-816.
15. S. Genovesi, L. Antolini, M. Giussani, F. Pieruzzi, S. Galbiati, M.G. Valsecchi, P. Brambilla, A. Stella, Usefulness of waist circumference for the identification of childhood hypertension, Journal of Hypertension, 26 (2008).
16. S. Lee, F. Bacha, N. Gungor, S.A. Arslanian, Waist circumference is an independent predictor of insulin resistance in black and white youths, The Journal of Pediatrics, 148 (2006) 188-194.
17. V. Hirschler, C. Aranda, M.d.L. Calcagno, G. Maccalini, M. Jadzinsky, Can Waist Circumference Identify Children With the Metabolic Syndrome?, Archives of Pediatrics & Adolescent Medicine, 159 (2005) 740-744.
18. C. Jung, N. Fischer, M. Fritzenwanger, H.R. Figulla, Anthropometric indices as predictors of the metabolic syndrome and its components in adolescents, Pediatrics international : official journal of the Japan Pediatric Society, 52 (2010) 402-409.
19. E.A. Sellers, G.R. Singh, S.M. Sayers, Large waist but low body mass index: the metabolic syndrome in Australian Aboriginal children, J Pediatr, 153 (2008) 222-227.
20. L.A. Moreno, I. Pineda, G. Rodríguez, J. Fleta, A. Sarría, M. Bueno, Waist circumference for the screening of the metabolic syndrome in children, Acta paediatrica (Oslo, Norway : 1992), 91 (2002) 1307-1312.
21. M.D. Jensen, D.H. Ryan, C.M. Apovian, J.D. Ard, A.G. Comuzzie, K.A. Donato, F.B. Hu, V.S.

Hubbard, J.M. Jakicic, R.F. Kushner, C.M. Loria, B.E. Millen, C.A. Nonas, F.X. Pi-Sunyer, J. Stevens, V.J. Stevens, T.A. Wadden, B.M. Wolfe, S.Z. Yanovski, 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults, Journal of the American College of Cardiology, 63 (2014) 2985-3023.

22. A. Afshin, M.B. Reitsma, C.J.L. Murray, Health Effects of Overweight and Obesity in 195 Countries, The New England journal of medicine, 377 (2017) 1496-1497.
23. G. Whitlock, S. Lewington, P. Sherliker, R. Clarke, J. Emberson, J. Halsey, N. Qizilbash, R. Collins, R. Peto, Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies, Lancet, 373 (2009) 1083-1096.
24. S. Yusuf, S. Hawken, S. Ôunpuu, L. Bautista, M.G. Franzosi, P. Commerford, C.C. Lang, Z. Rumboldt, C.L. Onen, L. Lisheng, S. Tanomsup, P. Wangai, F. Razak, A.M. Sharma, S.S. Anand, Obesity and the risk of myocardial infarction in 27 000 participants from 52 countries: a case-control study, The Lancet, 366 (2005) 1640-1649.
25. F.F. Casanueva, B. Moreno, R. Rodríguez-Azeredo, C. Massien, P. Conthe, X. Formiguera, V. Barrios, B. Balkau, Relationship of abdominal obesity with cardiovascular disease, diabetes and hyperlipidaemia in Spain, Clinical Endocrinology, 73 (2010) 35-40.
26. H. Gill, M. Mugo, A. Whaley-Connell, C. Stump, J.R. Sowers, The Key Role of Insulin Resistance in the Cardiometabolic Syndrome, The American Journal of the Medical Sciences, 330 (2005) 290-294.
27. G.M. Reaven, Diet and syndrome X, Current Atherosclerosis Reports, 2 (2000) 503-507.
28. P. Dandona, A. Aljada, A. Chaudhuri, P. Mohanty, R. Garg, Metabolic Syndrome, Circulation, 111 (2005) 1448-1454.
29. J.-P. DesprÉS, 10 Visceral Obesity, Insulin Resistance, and Dyslipidemia: Contribution of Endurance Exercise Training to the Treatment of the Plurimetabolic Syndrome, Exercise and Sport Sciences Reviews, 25 (1997).
30. P. Poirier, I. Lemieux, P. Mauriège, E. Dewailly, C. Blanchet, J. Bergeron, J.-P. Després, Impact of Waist Circumference on the Relationship Between Blood Pressure and Insulin, Hypertension, 45 (2005) 363-367.
31. C.S. Kuo, C.M. Hwu, S.C. Chiang, L.C. Hsiao, M.J. Weih, W.Y. Kao, S.H. Lee, C.F. Kwok, L.T. Ho, Waist circumference predicts insulin resistance in offspring of diabetic patients, Diabetes Nutr Metab, 15 (2002) 101-108.
32. M.-C. Pouliot, J.-P. Després, S. Lemieux, S. Moorjani, C. Bouchard, A. Tremblay, A. Nadeau, P.J. Lupien, Waist circumference and abdominal sagittal diameter: Best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women, The American journal of cardiology, 73 (1994) 460-468.
33. N. Barzilai, L. She, B.Q. Liu, P. Vuguin, P. Cohen, J. Wang, L. Rossetti, Surgical removal of visceral fat reverses hepatic insulin resistance, Diabetes, 48 (1999) 94-98.
34. P. Arner, Not all fat is alike, Lancet, 351 (1998) 1301-1302.
35. T.K.T. Lam, G.V.d. Werve, A. Giacca, Free fatty acids increase basal hepatic glucose production and induce hepatic insulin resistance at different sites, American Journal of Physiology-Endocrinology and Metabolism, 284 (2003) E281-E290.
36. G. Boden, X. Chen, J. Ruiz, J.V. White, L. Rossetti, Mechanisms of fatty acid-induced inhibition of glucose uptake, The Journal of Clinical Investigation, 93 (1994) 2438-2446.
37. M.E. Griffin, M.J. Marcucci, G.W. Cline, K. Bell, N. Barucci, D. Lee, L.J. Goodyear, E.W. Kraegen, M.F. White, G.I. Shulman, Free fatty acid-induced insulin resistance is associated with activation of protein kinase C theta and alterations in the insulin signaling cascade, Diabetes, 48 (1999) 1270-1274.
38. M. Ellmerer, M. Hamilton-Wessler, S.P. Kim, K. Huecking, E. Kirkman, J. Chiu, J. Richey, R.N.

Bergman, Reduced Access to Insulin-Sensitive Tissues in Dogs With Obesity Secondary to Increased Fat Intake, Diabetes, 55 (2006) 1769-1775.
39. M. Kabir, K.J. Catalano, S. Ananthnarayan, S.P. Kim, G.W.V. Citters, M.K. Dea, R.N. Bergman, Molecular evidence supporting the portal theory: a causative link between visceral adiposity and hepatic insulin resistance, American Journal of Physiology-Endocrinology and Metabolism, 288 (2005) E454-E461.
40. R.N. Bergman, S.P. Kim, I.R. Hsu, K.J. Catalano, J.D. Chiu, M. Kabir, J.M. Richey, M. Ader, Abdominal Obesity: Role in the Pathophysiology of Metabolic Disease and Cardiovascular Risk, The American Journal of Medicine, 120 (2007) S3-S8.
41. I.R. Hsu, E. Zuniga, R.N. Bergman, Pulsatile changes in free fatty acids augment hepatic glucose production and preserves peripheral glucose homeostasis, American Journal of Physiology-Endocrinology and Metabolism, 299 (2010) E131-E136.
42. L. Landsberg, Insulin-mediated sympathetic stimulation: role in the pathogenesis of obesity-related hypertension (or, how insulin affects blood pressure, and why), Journal of Hypertension, 19 (2001).
43. M. Snijder, R. van Dam, M. Visser, J. Seidell, What aspects of body fat are particularly hazardous and how do we measure them?, International Journal of Epidemiology, 35 (2005) 83-92.
44. S. Cook, P. Auinger, C. Li, E.S. Ford, Metabolic Syndrome Rates in United States Adolescents, from the National Health and Nutrition Examination Survey, 1999–2002, The Journal of Pediatrics, 152 (2008) 165-170.e162.
45. G.E. Duncan, S.M. Li, X.-H. Zhou, Prevalence and Trends of a Metabolic Syndrome Phenotype Among U.S. Adolescents, 1999–2000, Diabetes Care, 27 (2004) 2438-2443.
46. H.E. Bays, Adiposopathy, Journal of the American College of Cardiology, 57 (2011) 2461-2473.
47. V. Hirschler, M.I. Roque, M.L. Calcagno, C. Gonzalez, C. Aranda, Maternal Waist Circumference and the Prediction of Children's Metabolic Syndrome, Archives of Pediatrics & Adolescent Medicine, 161 (2007) 1205-1210.
48. S. Mottillo, K.B. Filion, J. Genest, L. Joseph, L. Pilote, P. Poirier, S. Rinfret, E.L. Schiffrin, M.J. Eisenberg, The Metabolic Syndrome and Cardiovascular Risk, Journal of the American College of Cardiology, 56 (2010) 1113-1132.
49. S. Bussler, M. Penke, G. Flemming, Y.S. Elhassan, J. Kratzsch, E. Sergeyev, T. Lipek, M. Vogel, U. Spielau, A. Körner, T. de Giorgis, W. Kiess, Novel Insights in the Metabolic Syndrome in Childhood and Adolescence, Hormone Research in Paediatrics, 88 (2017) 181-193.
50. C.L. Lafortuna, F. Adorni, F. Agosti, A. De Col, K. Sievert, W. Siegfried, A. Sartorio, Prevalence of the metabolic syndrome among extremely obese adolescents in Italy and Germany, Diabetes Research and Clinical Practice, 88 (2010) 14-21.
51. A.M. Lee, M.J. Gurka, M.D. DeBoer, Trends in Metabolic Syndrome Severity and Lifestyle Factors Among Adolescents, Pediatrics, 137 (2016) e20153177.
52. Are Metabolically Healthy Overweight and Obesity Benign Conditions?, Annals of Internal Medicine, 159 (2013) 758-769.
53. S. Bajaj, S. Fuloria, V. Subramaniyan, D.U. Meenakshi, S. Wakode, A. Kaur, H. Bansal, S. Manchanda, S. Kumar, N.K. Fuloria, Chemical Characterization and Anti-Inflammatory Activity of Phytoconstituents from Swertia alata, Plants (Basel, Switzerland), 10 (2021).
54. K. Samaras, N.K. Botelho, D.J. Chisholm, R.V. Lord, Subcutaneous and Visceral Adipose Tissue Gene Expression of Serum Adipokines That Predict Type 2 Diabetes, Obesity, 18 (2010) 884-889.
55. M. Kabir, D. Stefanovski, I.R. Hsu, M. Iyer, O.O. Woolcott, D. Zheng, K.J. Catalano, J.D. Chiu, S.P. Kim, L.N. Harrison, V. Ionut, M. Lottati, R.N. Bergman, J.M. Richey, Large Size Cells in the Visceral Adipose Depot Predict Insulin Resistance in the Canine Model, Obesity, 19 (2011) 2121-2129.
56. A.-L. Borel, J.-A. Nazare, J. Smith, N. Alméras, A. Tremblay, J. Bergeron, P. Poirier, J.-P. Després,

Improvement in insulin sensitivity following a 1-year lifestyle intervention program in viscerally obese men: contribution of abdominal adiposity, Metabolism, 61 (2012) 262-272.
57. M.G. Farb, S. Bigornia, M. Mott, K. Tanriverdi, K.M. Morin, J.E. Freedman, L. Joseph, D.T. Hess, C.M. Apovian, J.A. Vita, N. Gokce, Reduced Adipose Tissue Inflammation Represents an Intermediate Cardiometabolic Phenotype in Obesity, Journal of the American College of Cardiology, 58 (2011) 232-237.
58. K.A. Britton, J.M. Massaro, J.M. Murabito, B.E. Kreger, U. Hoffmann, C.S. Fox, Body Fat Distribution, Incident Cardiovascular Disease, Cancer, and All-Cause Mortality, Journal of the American College of Cardiology, 62 (2013) 921-925.
59. I.J. Neeland, S. Gupta, C.R. Ayers, A.T. Turer, J.E. Rame, S.R. Das, J.D. Berry, A. Khera, D.K. McGuire, G.L. Vega, S.M. Grundy, J.A.d. Lemos, M.H. Drazner, Relation of Regional Fat Distribution to Left Ventricular Structure and Function, Circulation: Cardiovascular Imaging, 6 (2013) 800-807.
60. J. Liu, C.S. Fox, D.A. Hickson, W.D. May, K.G. Hairston, J.J. Carr, H.A. Taylor, Impact of Abdominal Visceral and Subcutaneous Adipose Tissue on Cardiometabolic Risk Factors: The Jackson Heart Study, The Journal of Clinical Endocrinology & Metabolism, 95 (2010) 5419-5426.
61. J. Liu, C.S. Fox, D. Hickson, A. Bidulescu, J.J. Carr, H.A. Taylor, Fatty Liver, Abdominal Visceral Fat, and Cardiometabolic Risk Factors, Arteriosclerosis, thrombosis, and vascular biology, 31 (2011) 2715-2722.
62. C.S. Fox, J.M. Massaro, U. Hoffmann, K.M. Pou, P. Maurovich-Horvat, C.-Y. Liu, R.S. Vasan, J.M. Murabito, J.B. Meigs, L.A. Cupples, R.B. D'Agostino, C.J. O'Donnell, Abdominal Visceral and Subcutaneous Adipose Tissue Compartments, Circulation, 116 (2007) 39-48.
63. I.J. Neeland, A.T. Turer, C.R. Ayers, T.M. Powell-Wiley, G.L. Vega, R. Farzaneh-Far, S.M. Grundy, A. Khera, D.K. McGuire, J.A. de Lemos, Dysfunctional Adiposity and the Risk of Prediabetes and Type 2 Diabetes in Obese Adults, Jama, 308 (2012) 1150-1159.
64. R.K. Kalkhoff, A.H. Hartz, D. Rupley, A.H. Kissebah, S. Kelber, Relationship of body fat distribution to blood pressure, carbohydrate tolerance, and plasma lipids in healthy obese women, The Journal of Laboratory and Clinical Medicine, 102 (1983) 621-627.
65. K.V. Sathasivam, M. Haris, S. Fuloria, N.K. Fuloria, R. Malviya, V. Subramaniyan, Chemical Modification of Banana Trunk Fibers for the Production of Green Composites, Polymers, 13 (2021).
66. W. Bao, S.R. Srinivasan, W.A. Wattigney, G.S. Berenson, Persistence of Multiple Cardiovascular Risk Clustering Related to Syndrome X From Childhood to Young Adulthood: The Bogalusa Heart Study, Archives of Internal Medicine, 154 (1994) 1842-1847.
67. W. Chen, S.R. Srinivasan, S. Li, J. Xu, G.S. Berenson, Clustering of Long-term Trends in Metabolic Syndrome Variables from Childhood to Adulthood in Blacks and Whites: The Bogalusa Heart Study, American Journal of Epidemiology, 166 (2007) 527-533.
68. I. Janssen, S.B. Heymsfield, D.B. Allison, D.P. Kotler, R. Ross, Body mass index and waist circumference independently contribute to the prediction of nonabdominal, abdominal subcutaneous, and visceral fat, The American journal of clinical nutrition, 75 (2002) 683-688.
69. S.M. Barreiro, H.O. Santos, R.P.F. Cruz, P.C. Nahas, L.T. Rossato, F.L. Orsatti, E.P. de Oliveira, Adductor pollicis muscle thickness has a low association with lean mass in women, Clinical Nutrition, 37 (2018) 1759-1761.
70. L.S. Limirio, L.T. Rossato, C.D. Barbosa, K.R.C. Teixeira, P.C. Nahas, F.M.S. de Branco, F.M. Martins, R.S. Nomelini, E.F.C. Murta, F.L. Orsatti, E.P. de Oliveira, Body Mass Index, waist circumference or sagittal abdominal diameter: Which parameter is better correlated with body fat changes in postmenopausal women after combined training protocol?, Clinical Nutrition ESPEN, 38 (2020) 192-195.
71. N.F. Krebs, M.S. Jacobson, Prevention of pediatric overweight and obesity, Pediatrics, 112 (2003)

424-430.
72. V. Subramaniyan, S. Fuloria, O. Porwal, A. Aaleem, S. Jafarullah, M. Sekar, K. Sathasivam, U.M. Dhana Lekshmi, U. Kumari, V. Kumar, Y.-S. Wu, N. Fuloria, Dental Infections and Antimicrobials, Journal of Drug and Alcohol Research, 10 (2021) 236121.
73. M. Barzin, F. Hosseinpanah, S. Fekri, F. Azizi, Predictive value of body mass index and waist circumference for metabolic syndrome in 6–12-year-olds, Acta Paediatrica, 100 (2011) 722-727.
74. S.S. Sun, R. Liang, T.T. Huang, S.R. Daniels, S. Arslanian, K. Liu, G.D. Grave, R.M. Siervogel, Childhood obesity predicts adult metabolic syndrome: the Fels Longitudinal Study, J Pediatr, 152 (2008) 191-200.
75. H.M. Farin, F. Abbasi, G.M. Reaven, Comparison of body mass index versus waist circumference with the metabolic changes that increase the risk of cardiovascular disease in insulin-resistant individuals, The American journal of cardiology, 98 (2006) 1053-1056.
76. R. Kelishadi, S.R. Cook, M.E. Motlagh, M.M. Gouya, G. Ardalan, M. Motaghian, R. Majdzadeh, M.A. Ramezani, Metabolically obese normal weight and phenotypically obese metabolically normal youths: the CASPIAN Study, Journal of the American Dietetic Association, 108 (2008) 82-90.
77. S.P. Garnett, L.A. Baur, S. Srinivasan, J.W. Lee, C.T. Cowell, Body mass index and waist circumference in midchildhood and adverse cardiovascular disease risk clustering in adolescence, The American journal of clinical nutrition, 86 (2007) 549-555.
78. S. Ugrappa, A. Jain, A. Bhargava, N. Fuloria, S. Fuloria, A search in the surge of treatment for COVID-19 patients: A narrative literature review, International Journal of Research in Pharmaceutical Sciences, 11 (2020) 822-831.
79. C. Andersen, D. Aguilar, J. Jones, C. Blesso, T. Al-Sarraj, C. Dugan, J. Barona, M.-L. Fernandez, Increased body mass index adversely affects dyslipidemias, blood pressure and inflammation in men and women with metabolic syndrome (LB365), The FASEB Journal, 28 (2014) LB365.