

Editorial

Metabolic Syndrome and Nonalcoholic Fatty Liver Disease

Contemporary concerns

NAMS-PGI Centre of Tele-medicine and Tele-education organized a Symposium on Hepatology with a sharper focus on Nonalcoholic Fatty Liver Disease (NAFLD). Selected contributions covering a wide range of subjects including epidemiology, natural history, pathophysiology, clinical profile, laboratory diagnosis, and diagnostic imaging of NAFLD along with presentations on some of its sequelae eg. hepatocellular carcinoma, and management of hepatic failure using artificial liver support systems and liver transplantation, have been selected for the current issue of the Annals. The contributors are recognized authorities on the subjects covered, and we appreciate the efforts put in by all of them to provide a state-of-art account which should be of equal interest to postgraduate residents as well as practicing specialists.

In the perspective of an extensive coverage of NAFLD, there are a few unresolved questions which require future research. Rightly considered as a frequently encountered component of metabolic syndrome, the excessive accumulation of fat in hepatocytes is

generally attributed to central (trunkal) obesity and large influx of free fatty acids (FFA) to the liver. Insulin resistance is a key feature in most of the cases. Although there is an emerging consensus regarding the diagnostic criteria of metabolic syndrome in adults incorporating ethnic-specific and gender-related cut-offs for waist circumference, to apply these criteria *mutatis mutandis* to the pediatric, and especially adolescent, age groups is neither evidence-based nor clinically justifiable. The issue has assumed considerable significance primarily due to new insights: (i) rising prevalence of obesity and other components of metabolic syndrome including NAFLD in the pediatric and adolescent age groups, and (ii) age-related divergence of BMI and waist circumference as an indicator of subsequent development of metabolic syndrome.

Pediatric Metabolic Syndrome Working Group, convened by the US National Institute for Child Health and Human Development, had been assigned the task of developing a more precise definition of metabolic syndrome in pediatric practice. Some of the trends seem to be clearly

emerging as a result of several recent studies. A cohort of 1479 (M/F : 740/739) children, age 5-15 years, was studied (1). In a sub-group of 505 over weight or obese children and adolescents, relationship between anthropomorphic measurements and metabolic as well as cardiovascular risk factors was investigated and compared with similar data in 974 healthy, normal weight children. Obese children or adolescents with a waist circumference above the 90th percentile for their age had a 13-fold higher risk of having two metabolic risk factors, compared with the control group whose waist circumference was below the 90th percentile. Overweight, but not obese, subjects with waist circumference above the 90th percentile had a sevenfold higher risk while overweight children with waist circumference below the 90th percentile had no greater risk. Combining waist-to-height ratio with BMI, odds ratio of metabolic syndrome was 12.11 in those with obese BMI as well as waist/height ratio > 0.5 while it was 8.16 in those with overweight BMI and waist/height ratio > 0.5. Most significantly, it was concluded that waist-to-height ratio alone could serve as an important determinant of metabolic and cardiovascular risk especially in the pediatric and adolescent age groups.

This simple and easy-to-measure parameter (waist/height ratio) is not dependent on ethnicity nor does it require sophisticated instrumentation. In contrast to the simplicity of this recommendation,

the complexity of current situation is outlined in another study wherein 27 articles dealing with diagnosis of metabolic syndrome in adolescents were reviewed, and 46 different definitions of metabolic syndrome were found (2)!

What is the clinical advantage of early diagnosis of childhood obesity? In a study conducted to determine whether childhood obesity predicts adult metabolic syndrome, data from a cohort of 151 subjects with metabolic syndrome were compared with those from 154 matched controls without the syndrome (3). The objective of the study was to determine if there was any age in childhood at which waist circumference diverged in those who subsequently develop metabolic syndrome, compared with those who do not. In male subjects, the first difference in waist circumference was observed at 8 years of age while in girls the determinant age was 13 years.

How does it relate to Pediatric Non-alcoholic Fatty Liver Disease (PNAFLD)? A recent study suggests that PNAFLD is strongly associated with multiple cardiovascular risk factors. Moreover, the prevalence of metabolic syndrome in children and adolescents with NAFLD is *twice* that seen in equally obese youths without the hepatic disease. These new findings from a 300-patient case-control study emphasize the significance of routine screening for NAFLD in obese youth with a view to preventing its progression to

hepatic failure in adulthood. Furthermore, cardiovascular risk profile demonstrated in this study raises the strong possibility that youths with NAFLD may be predisposed to highly premature cardiovascular morbidity and mortality (4).

The direction is clear : there are early childhood indicators which portend the subsequent development of cardiovascular and metabolic risk factors, and that the key to management lies in **prevention**. Life style choices must be inculcated at an early age. In the South-East Asian and the Indian context, it is important to recognize that insulin resistance becomes apparent in infancy, possibly due to the fact that intra-uterine growth retardation in pregnancy and catch-up growth in early infancy result in metabolic programming leading to higher risk of various components of metabolic syndrome in adult life. There is thus increasing evidence linking maternal malnutrition, low birth weight, and nutritional programming in early life, with the development of a

constellation of metabolic (including NAFLD) and cardiovascular diseases in adult life, with the common denominator of insulin resistance (5). It is therefore axiomatic that a balanced nutrition during pregnancy followed by healthy life style choices during childhood constitute a sound public health strategy. Failure to adopt, and implement, such an approach is likely to add to the disease burden including type 2 diabetes, hypertension, cardiovascular diseases and NAFLD. Neither society nor country's health system can bear the resultant escalating costs of health care. Prevention must be viewed as a life and death matter, and therefore a more pressing priority than ever before.

As the American psychiatrist Karl Menninger said, "What we do to children, they will do to society". In the South-East Asian context, it may be modified to state, "What we do to pregnant mothers and children, they will do to society".

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References :

1. Maffeis C, Banzato C, Talamini G and Obesity Study Group of the Italian Society of Pediatric Endocrinology and Diabetology (2008). Waist-to-Height Ratio, a Useful Index to Identify High Metabolic Risk in Overweight Children. *J Pediatr*. **152** ; 207-213.
2. Cook S, Auinger P, Li C, Ford ES (2008). Metabolic Syndrome Rates in United States Adolescents, from the National Health and Nutrition Examination Survey, 1999-2002. *J Pediatr*. **152**; 165-170.
3. Sun SS, Liang R, Huang TTK, Daniels SR, Arslanian S, Liu K, Grave GD,

- Siervogel RM (2008). Childhood Obesity Predicts Adult Metabolic Syndrome : The Fels Longitudinal Study. *J Pediatr*. **152** ; 191-200.
4. Cook S, Schwimmer JB (2008). Pediatric fatty liver boosts cardiovascular risk. Paper presented at Annual Conference of American Heart Association.
5. Bajaj JS, Bajaj M (2004). Hepatic Fat and Insulin Resistance : Causes and consequences of Non-alcoholic Fatty Liver Disease. In : Non-Alcoholic Fatty Liver Disease. Sarin SK, Sood OP, eds. 175-197.