

ORIGINAL ARTICLE

PREVALENCE OF THE METABOLIC SYNDROME AND ITS COMPONENT ABNORMALITIES AMONG SCHOOL AGE PAKISTANI CHILDREN

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Background: Concurrence of central adiposity, hypertension, hyperglycaemia, and atherogenic dyslipidaemia has been termed as the metabolic syndrome. High prevalence of the syndrome has been reported globally over the last decade. **Methods:** This cross-sectional study is based on a sample of eighty five children, ranging in age from six to twelve years. After parental consent, height, weight, waist circumference, and blood pressure were measured and investigation requests for fasting plasma glucose and fasting lipid profile were given. Children with known metabolic disorders, and those using metabolic-profile-altering medication were excluded. **Results:** The prevalence of metabolic syndrome, according to the various definitions, varied from as high as 16.5% (95% CI: 9.3–26.1%) to as low as 1.8% (95% CI: 0.03–6.4%). The most prevalent of the component abnormalities was blood pressure above 90th percentile, positive in 54% (95% CI: 43.0–65.0). HDL-c was low (≤ 1.3 mmol/L) in 36.5% (95% I: 26.3–47.6%), and waist circumference high ($>75^{\text{th}}$ percentile) in 30.6% (95% CI: 21.0–41.5%). Both systolic blood pressure and triglycerides to HDL-cholesterol ratio showed a linear trend of increasing with increasing quartiles of waist and body mass index (BMI). **Conclusion:** Depending on the cut-off values used for defining the component abnormalities, the metabolic syndrome may be quite prevalent in this population. Waist circumference above 75th percentile and even a single reading of blood pressure above 90th percentile should be considered a warning sign, indicating further investigation and lifestyle interventions.

Keywords: Metabolic Syndrome, cardio-metabolic risk, central obesity, waist circumference, dyslipidaemia

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INTRODUCTION

Concurrence of hypertension, hyperglycemia, and hyperuricemia and the relationship between body fat distribution and the risk of developing diabetes and cardiovascular disease was noted by researchers in early and mid-twentieth century^{1,2}, association with hyperinsulinemia having been reported in the seventies³.

Gerald M. Reaven, in his 1988 Banting Lecture⁴, highlighted the relationship between insulin resistance, hyperinsulinemia, and hypertension and suggested that it could be a causal one. Later, he described this constellation of anomalies as insulin resistance syndrome.⁵

The metabolic syndrome as a diagnostic entity, with specific components and cut points, was introduced by the world health organization (WHO) in 1998⁶, but a wider acceptance has been given to the definition by United States Adult Treatment Panel III in May, 2001.⁷ The entity has evolved through a rather tumultuous run of nomenclatures: syndrome X, Reaven's syndrome, insulin resistance syndrome, atherothrombotic syndrome⁸ are some of the famous names it has held in the past, although it has also been referred

to as dysmetabolic syndrome⁹, and hypertriglyceridemic waist.⁹

The clinical and biochemical abnormalities of the metabolic syndrome are markers of insulin resistance which results in compensatory hyperinsulinemia, hypertension, dyslipidemia, and cardiovascular disease.¹¹ This constellation of abnormalities has also been found to associated with pro-thrombotic and pro-inflammatory states.¹²

Since the turn of the century, the world has been reported to be in the grips of a pandemic of the metabolic syndrome¹², and a lot of studies from all over the world have reported high prevalence of this syndrome.¹³ Using Gerald M. Reaven's words, this rather huge 'burst of creative activity' regarding the prevalence of the metabolic syndrome in recent years has proved to be of little practical assistance to the clinician.¹³

At least six various definitions of the metabolic syndrome in children have been used^{14–20}, with varying cut-offs for the five component clinical and biochemical abnormalities: fasting blood glucose (FBG), central obesity, triglycerides, high density lipoprotein cholesterol (HDL-c), and blood pressure (Table-1), some of which would tend to make the diagnostic criteria more specific

and would be less sensitive in detecting any potential opportunities of timely intervention for the clinician.

There is also some serious debate going on about the very existence of an entity like the metabolic syndrome.^{13,21} Irrespective of the nature or the truth of the syndrome, the fact remains that all its component abnormalities have independently, and repeatedly, shown to carry an increased risk of both cardiovascular disease and of diabetes mellitus.²² Metabolic syndrome, for the practicing physicians, can only serve as a marker of heightened cardio-metabolic risk, directing any interventional efforts, a function that can be most effectively provided by the easiest to measure component abnormality alone.

Lifestyles and food habits in Pakistan have been changing over the decades, at pace with the global socio-cultural and economic change. Children are especially influenced by the wide spread promotion and availability of fast foods and carbonated drinks.

Peshawar is no exception to this process of meta-change and, as clinicians, balancing the focus of practice between individual and public health aspects of care has become imperative. This necessitates insights into the health status of our population regarding the burden of cardio-metabolic risks.

This study was planned to estimate the prevalence of the metabolic syndrome according to its various definitions and to assess the clinical usefulness of its various component abnormalities, as defined by the cutoff points of various definitions, in correctly assessing cardio-metabolic risk, as indicated by biochemical markers of such risk.

MATERIAL AND METHODS

In this cross sectional study a sample of eighty five school age Pakistani children was chosen from the families of the clientele of the primary author's clinic, accrued over a period of 10 months in 2011. Families of children with known diabetes or lipid disorders were excluded. The study was approved by the internal review panel of Kabir Medical College.

The children, after parental consent, had a general physical examination including height, weight, waist circumference, and blood pressure measurements. Information about their food habits and lifestyle was collected by interviewing the child along with the parent. Waist was measured at a point midway between the lowest ribs laterally and the iliac crest, with the child standing.

Investigation requests were given to the parents. Early morning fasting blood glucose, triglycerides, and high density lipid cholesterol were recommended, the child fasting overnight.

Based on an empirical estimate of 5% prevalence of the Metabolic Syndrome²³, in order to estimate the population proportion with a 5% margin of error, a sample size of 73 would be required for a confidence level of 95%.²⁴

Data were entered in the computer using Epidata software.²⁵ For calculating and comparing proportions and for other statistical analysis, R version 2.1.3²⁶, and Stata version 8.2²⁷ software programs have been used.

Means±standard deviations are reported as summary measures for normally distributed continuous variables while medians with median absolute deviation (MAD) are reported for continuous variables with non-normal distributions. Proportions are reported as percentages. Two group comparisons regarding continuous variables are done using *t* tests for independent samples while Z approximations of binomial distributions have been used to compare two groups on a categorical variable. Pearson's Product-Moment Correlation Coefficient has been used to assess correlations between continuous variables. All tests of significance are two-tailed and a significance level of 0.05 has been used.

RESULTS

Out of these 85 children 42 (49.4%) were male while 43 (50.6%) were female. More than 80% of the participants were 10 years of age or less (Table-2).

The Mean weight of the participants was 29.6±10.4 kg, with no significant difference in weight between the two genders ($p=.86$). In fact none of the anthropometric measurements was significantly different between the genders (Table-2).

The median of BMI-for-Age percentiles for the sample was 31.6, with a median absolute deviation of 27.8. Based on the latest recommended cut-off points²⁸, 9.5% of these children were obese while 8.3% were overweight, with a total of 17.8% being at or above 85th percentile for BMI-for-Age. More than 20% were below the 5th percentile of BMI for age, with a total of 38% falling in the dysnutrition range, being either above or below normal (Table-3).

Twenty six (30.6%) of the participating children, based on waist circumference percentile values reported by McCarthy *et al*²⁹, had their waist circumference above 75th percentile for age and gender. Twelve (46.2%) of these were male while 14 (53.8%) were female; the difference being

statistically non-significant (one sample proportions test $z = -0.8185, p = .41$).

Mean of triglycerides for this sample was 0.67 ± 0.27 mmol/L, the range being 0.21–1.79 mmol/L. There was no difference between the two genders regarding triglyceride levels ($p = .40$).

Mean of HDL-c for these children was 1.4 ± 0.3 , ranging from 0.41–2.12, again the difference was not statistically significant ($p = .93$) (Table-4).

The most sensitive criteria for the diagnosis of metabolic syndrome were those of de Ferranti *et al*¹⁵, according to which, 16.5% (95% CI: 9.3–26.1) of this sample are positive for metabolic syndrome. The criteria used by Ford *et al*¹⁸ labelled 2.4% (95% CI: 0.3 – 8.2%) as positive. Cruz *et al*¹⁶, Cook *et al*¹⁴, Weiss *et al*¹⁷, and the International Diabetes Federation (IDF)¹⁹ criteria detected 1.8% (95% CI: 0.03–6.4%) as positive. While estimating the prevalence of the metabolic syndrome, two of the criteria, those of Cruz *et al*¹⁶, and Weiss *et al*¹⁷, could be applied only partially, because of the lack of glucose tolerance test data. Hence the prevalence values reported for these criteria are underestimates of the actual values (Table-5).

Regarding individual components, the most prevalent abnormality was that of blood pressure

which, either systolic or diastolic, was above 90th percentile for age and gender in 54% of these children (95% CI: 43.0 – 65.0), followed by HDL-c (≤ 1.3 mmol/L) in 36.5% (95% I: 26.3–47.6%) of cases, and waist circumference ($>75^{\text{th}}$ percentile for age and gender) in 30.6% (95% CI: 21.0– 41.5%) (Table-6).

Triglycerides to HDL-c ratio above 75th percentile showed significant linear trend of increasing both with increasing quartiles of waist (chi square=6.41, $p = .011$) and those of bmi (chi square=5.34, $p = .021$).

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Table-1: A range of the published definitions of metabolic syndrome in children*

Component	MS Positive if \geq Three of the Risk Factors are Positive					MS Positive if WC is high along with any other 2 or >
	Cook <i>et al</i> ¹⁴	de Ferranti <i>et al</i> ¹⁵	Cruz <i>et al</i> ¹⁶	Weiss <i>et al</i> ¹⁷	Ford <i>et al</i> ¹⁸	
FBS	≥ 110 mg/dL (6.1 mmol/L)	≥ 6.1 mmol/L (≥ 110 mg/dL)	Impaired glucose tolerance (ADA criterion)	Impaired glucose tolerance (ADA criterion)	≥ 110 mg/dL (≥ 6.1 mmol/L) (additional analysis with ≥ 100 mg/d; 5.6 mmol/L)	6Yrs-<10: No Cutoff 10Yrs-<16: ≥ 5.6 mmol/L (≥ 100 mg/dL) ≥ 16 : ≥ 5.6 mmol/L (≥ 100 mg/dL)
Central Obesity (Waist Circumference)	WC $\geq 90^{\text{th}}$ percentile (age- and sex-specific, NHANES III)	WC $>75^{\text{th}}$ percentile	WC $\geq 90^{\text{th}}$ percentile (age-, sex- and race-specific, NHANES III)	BMI -Z score ≥ 2.0 (age- and sex-specific)	WC $\geq 90^{\text{th}}$ percentile (sex-specific, NHANES III)	6Yrs-<10: $\geq 90^{\text{th}}$ Percentile (while can't diagnose MS!) 10Yrs-<16: $\geq 90^{\text{th}}$ Percentile OR Adult!! ≥ 16 Yrs: WC ≥ 94 cm Male, 80cm Female
Triglycerides	≥ 110 mg/dL (≥ 1.24 mmol/L) (age-specific, NCEP)	≥ 1.1 mmol/L (≥ 100 mg/dL)	$\geq 90^{\text{th}}$ percentile (age- and sex-specific, NHANES III)	Triglycerides $>95^{\text{th}}$ percentile (age-, sex- and race-specific, NGHS)	Triglycerides ≥ 110 mg/dL (≥ 1.24 mmol/L) (age-specific, NCEP)	6Yrs-<10: No Cutoff 10Yrs-<16: ≥ 1.7 mmol/L (≥ 150 mg .dL) ≥ 16 Yrs: ≥ 1.7 mmol/L (≥ 150 mg .dL)
HDL	HDL-C ≤ 40 mg/dL (1.03 mmol/L) (all ages/sexes, NCEP)	HDL-C <1.3 mmol/L (<50 mg/dL)	HDL-C $\leq 10^{\text{th}}$ percentile (age- and sex-specific, NHANES III)	HDL-C $<5^{\text{th}}$ percentile (age-, sex- and race-specific, NGHS)	HDL-C ≤ 40 mg/dL (1.03 mmol/L) (all ages/sexes, NCEP)	6Yrs-<10: No Cutoff 10Yrs-<16: <1.03 mmol/L (40 mg/dL) for all ≥ 16 Yrs: <1.03 mmol/L (40 mg/dL) for Males <1.29 mmol/L (50 mg/dL) for Females
BP	$\geq 90^{\text{th}}$ percentile (age-, sex- and height-specific, NHBPEP)	$>90^{\text{th}}$ percentile	$>90^{\text{th}}$ percentile (age-, sex- and height-specific, NHBPEP)	$>95^{\text{th}}$ percentile (age-, sex- and height-specific, NHBPEP)	$\geq 90^{\text{th}}$ percentile (age-, sex- and height-specific, NHBPEP)	6Yrs-<10: No Cutoff 10Yrs-<6: $\geq 130/85$ mmHg ≥ 16 Yrs: $\geq 130/85$ mmHg

*From: The IDF consensus definition of metabolic syndrome in children and adolescents¹⁹

Table-2: Distribution of Anthropometric Variables (Mean (SD)) and Age-wise comparisons between Genders (p-Values for 2 sided independent samples t-tests)

Age in Years (n, %)	6 (8, 9.4)			7 (16, 18.8)			8 (15, 17.6)			9 (12, 14.1)			10 (18, 21.2)			≥11 (16, 18.8)		
	M (3, 37.5)	F (5, 62.5)	p	M (7, 43.8)	F (9, 56.2)	p	M (9, 60.0)	F (6, 40.0)	p	M (4, 33.3)	F (8, 66.7)	p	M (9, 50.0)	F (9, 50.0)	p	M (10, 62.5)	F (6, 37.5)	p
Weight (kg)	21.0±3.0	21.0±1.4	>.9	24.0±6.4	23.8±1.4	.92	23.3±4.5	22.0±2.6	.53	33.3±9.7	32.2±8.0	.85	31.8±11.1	35.1±9.5	.50	39.3±13.5	40.2±11.8	.89
Height (cm)	117.3±7.8	119±1.4	.68	124.1±8.3	124.2±3.9	.98	126.4±4.8	125.0±6.1	.62	133.2±2.8	134.0±7.0	.84	135.9±7.0	141.9±9.7	.15	143.4±9.2	145.0±7.9	.73
BMI (kg/m ²)	15.3±1.7	15.0±0.9	.80	15.5±3.3	15.4±1.1	.95	14.6±2.5	14.0±0.7	.63	18.7±5.2	17.8±2.9	.69	16.8±4.1	17.2±3.1	.84	18.9±5.6	19.0±5.0	.99
Waist (cm)	53.7±6.5	56.6±1.1	.34	56.8±9.6	62.3±3.0	.13	56.4±4.8	57.8±3.3	.55	64.2±9.0	64.2±7.8	>.9	60.2±10.1	67.8±8.6	.11	69.3±15.0	68.5±12.1	>.9
Hip (cm)	62.3±6.6	65.4±3.1	.39	63.8±8.8	69.6±4.5	.11	63.9±4.3	65.2±3.6	.56	72.8±9.7	74.4±6.6	.74	72.1±9.6	78.6±7.7	.14	78.3±13.4	80.3±10.2	.76
Waist-Hip Ratio	0.86±0.07	0.87±0.05	.90	0.89±0.07	0.90±0.04	.78	0.88±0.04	0.89±0.04	.82	0.88±0.04	0.86±0.05	.51	0.83±0.07	0.86±0.07	.38	0.88±0.07	0.85±0.05	.36
Waist-Height Ratio	0.46±0.04	0.47±0.01	.46	0.46±0.07	0.50±0.02	.12	0.45±0.03	0.46±0.03	.29	0.48±0.07	0.48±0.04	.89	0.44±0.06	0.48±0.05	.18	0.48±0.09	0.47±0.08	.82

*Age groups 11 (n=12) and 12 (n=4) have been combined for analysis because of low number in 12 Years age group

Table-3: Weight Status as assessed with BMI-for-Age Measurement*

Class	Definition: BMI-for-Age Percentile	Male (row %)	Female (row %)	Total (column %)
Obese	≥95 th	6 (75)	2 (25)	8 (9.52)
Overweight	≥85 th and <95 th	5 (71.43)	2 (28.57)	7 (8.33)
Normal	Between 5 th and 85 th	17 (32.69)	35 (67.31)	52 (61.90)
Underweight	Below 5 th	14 (82.35)	3 (17.65)	17 (20.24)
Total		42 (50)	42 (50)	84 (100.00)

*Data for 84 children only

Table-4: Summary of Biochemical Markers of Cardio-metabolic Risk (Mean±SD) and Age-wise comparisons between Genders (p-Values for 2 sided independent samples t-tests)*. All results are in mmol/L.

Age in Years (n, %)	6 (8, 9.4)			7 (16, 18.8)			8 (15, 17.6)			9 (12, 14.1)			10 (18, 21.2)			≥11 (16, 18.8)		
	M (3, 37.5)	F (5, 62.5)	p	M (7, 43.8)	F (9, 56.2)	p	M (9, 60.0)	F (6, 40.0)	p	M (4, 33.3)	F (8, 66.7)	p	M (9, 50.0)	F (9, 50.0)	p	M (10, 62.5)	F (6, 37.5)	p
T. Cholesterol	3.71±0.24	4.02±0.48	.34	3.68±1.12	4.26±0.47	.18	4.30±0.49	4.27±0.49	.92	4.19±0.83	4.02±0.45	.64	4.23±0.33	4.42±0.64	.45	4.34±0.48	4.20±0.49	.59
HDL-c	1.17±0.33	1.26±0.12	.59	1.30±0.44	1.42±0.25	.52	1.59±0.29	1.50±0.21	.55	1.59±0.45	1.33±0.26	.22	1.37±0.29	1.41±0.30	.79	1.31±0.36	1.42±0.25	.53
LDL-c	2.25±0.12	2.6±0.43	.26	2.07±0.61	2.54±0.47	.10	2.43±0.48	2.47±0.55	.87	2.25±0.46	2.34±0.34	.68	2.54±0.44	2.66±0.49	.61	2.64±0.56	2.31±0.62	.29
TAG	0.57±0.35	0.65±0.15	.66	0.62±0.18	0.67±0.19	.60	0.48±0.19	0.60±0.26	.33	0.53±0.32	0.78±0.13	.08	0.67±0.25	0.78±0.32	.43	0.87±0.46	0.66±0.07	.29
FBS	4.67±0.85	4.2±0.33	.29	4.08±0.81	4.3±0.19	.45	4.68±0.60	4.13±0.35	.07	4.8±0.14	4.4±0.33	.04 [†]	4.67±0.22	4.48±0.28	.13	4.73±0.56	4.93±0.61	.50
TAG-HDL-c Ratio	0.59±0.54	0.53±0.16	.82	0.52±0.17	0.50±0.22	.88	0.31±0.16	0.42±0.25	.32	0.34±0.16	0.60±0.14	.01 [†]	0.52±0.27	0.57±0.26	.71	0.76±0.51	0.48±0.13	.22
HDL-c, LDL-c Ratio	0.52±0.17	0.49±0.05	.69	0.62±0.11	0.58±0.17	.59	0.68±0.21	0.63±0.15	.62	0.72±0.26	0.58±0.14	.22	0.56±0.19	0.55±0.16	.87	0.54±0.27	0.66±0.25	.38

*M: Male; F: Female; T. Cholesterol: Total Cholesterol; HDL-c: High Density Lipoprotein Cholesterol; LDL-c: Low Density Lipoprotein Cholesterol; FBS: Fasting Blood Glucose, [†]: Statistically significant

Table-5: Prevalence of Metabolic Syndrome according to its various definitions

Definition	Prevalence	95% Confidence Interval
de Ferranti <i>et al.</i> Circulation, 2004; 110, 2494-97	16.47%	9.3–26.1%
Ford <i>et al.</i> Diabetes Care, 2005; 28, 871-81	2.35 %	0.3–8.2%
Weiss <i>et al</i> * N Engl J Med, 2004; 350, 2362-74	1.18%	0.03–6.4%
Cook <i>et al.</i> Arch Pediatr Adolesc Med, 2003; 157, 821-7	1.18%	0.03–6.4%
Cruz <i>et al.</i> * J Clin Endocrinol Metab, 2004; 89, 108-13	1.18%	0.03–6.4%
International Diabetes Federation 2007	1.18%	0.03–6.4%

*reported prevalence values are underestimates as Impaired Glucose Tolerance data were not available.

Table-6: Prevalence of individual components of the definition of Metabolic Syndrome by de Ferranti *et al*¹⁵

Component	Cut-off	Prevalence	95% Confidence Interval
Blood Pressure	Either >90 th Percentile	54.1%	43.0–64.9%
HDL-c	<1.3 mmol/L	36.5%	26.3–47.6%
Waist Circumference	>75 th Percentile	30.6%	21.0–41.5%
Triglycerides	≥1.1 mmol/L	5.9%	1.9–13.2%
Fasting Blood Glucose	≥6.1 mmol/L	1.2%	0–6.3%

DISCUSSION

Metabolic syndrome, as a diagnostic entity in clinical settings, unlike its possible heuristic value in basic

research, is useful only as a marker of increased cardiometabolic risk and as an indicator of the need for further exploration and lifestyle intervention. In

this respect, its role is that of a screening test, and should fulfil the criteria for a good screening test being helpful in detecting vulnerability for a long term problem, that is cardiometabolic disease in this case, at a stage when prevention can matter; and identifying risk factors that increase the likelihood of developing clinical disease. In this capacity, it can provide clinically useful information that may be important in preventing a disease, or lessening its impact, by modifying the risk factors.³⁰

The diseases in question, diabetes and coronary heart disease, constitute major burden of disease across the world³¹⁻³³, resulting in significant morbidity and mortality. Lifestyle change and dietary interventions have been proved to be effective in preventing them, in delaying their onset, and in preventing or delaying their complications³⁴.

A good screening test should be capable of detecting a high proportion of disease in its preclinical state, be safe to administer, be reasonable in cost, lead to demonstrated improved health outcomes, be widely available, and the interventions that follow should lead to positive outcomes.³⁵

For an intervention as harmless as lifestyle and dietary advice, the clinicians will look for a test that is the most sensitive in detecting cardiometabolic vulnerabilities as the intervention does not carry any potential harm and is beneficial even in false positive scenarios.

The authors find the IDF criteria for the diagnosis of the metabolic syndrome too specific to be useful for routine preventive initiatives in a paediatric practice. Such specificity may be necessary for basic research aimed at studying the bio-physiological and bio-molecular basis of the clustering of these abnormalities as costly biomedical investigations will be involved in that scenario. In the context of clinical practice aimed at early detection and prevention of cardiometabolic vulnerabilities, such specificity is not only unnecessary but may actually be harmful.

These specific criteria will bring only one of these children to attention as being in need for any further investigation or intervention, compared to fourteen by the most sensitive of these criteria, an incredibly high difference. With the global epidemic of cardiometabolic risk going on, this difference can very well serve as an Index of procrastination.

As routine investigation in the context of preventive care is neither recommended³⁶⁻³⁹ nor possible in many economies, simple clinical measures indicating higher risk become all the more relevant. It is important to note in the results of this study that the most prevalent of the markers of heightened cardiometabolic risk, Waist Circumference above 75th percentile and Blood

Pressure, are routine physical clinical measurements. With these simple measurements serving the purpose of selecting children and families for lifestyle interventions, any costly investigation would be unnecessary for preventive work aimed at reducing the prevalence of cardiometabolic risk in paediatric clinics.

The very high proportion of children showing blood pressure above 90th percentile may have resulted from the fact that all readings of blood pressure were taken on the same day and same session. In this context this may be a systematic error. Triglycerides to HDL-c ratio, a marker of increased cardiometabolic risk, showed a significant linear trend with increasing waist circumference and BMI. Although these findings needs to be confirmed by specially designed studies, it can be recommended that waist circumference above 75th percentile should be an indication for a full assessment of cardiometabolic risk in a child.

As the sample was selected from a private clinic clientele, the families were relatively affluent and hence the generalization of the findings may be questionable.

CONCLUSION

Waist circumference above 75th percentile should be considered as a warning sign, indicating further assessment of cardiometabolic risk and for initiating lifestyle intervention and dietary advice for the child and the family. While the debate regarding the metabolic syndrome may continue, which is how science happens, early warning signs like these are always valuable aids in clinical practice and serve as reminders to balance preventive and promotive components of clinical practice with the curative one.

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