10.5005/jp-journals-10039-1162

ORIGINAL ARTICLE

# Conservatively Treated Spinal Tuberculosis in Children: Ambulatory Chemotherapy

**Myung-Sang Moon**


## ABSTRACT

**Introduction:** To assess the chronological changes of the disease-related kyphosis after chemotherapy alone, and secondly to clarify the role of growth cartilage in the healed lesion on kyphosis change.

**Materials and methods:** A total of 101 children with spinal tuberculosis in various stages of disease processes, aged 2 to 15 years, were the subject materials. They were treated with two different chemotherapy formulas; before 1975, 18 months of triple chemotherapy [isoniazid (INH), paraaminosalicylic acid (PAS), and Streptomycin], and from 1976, 12 months of triple chemotherapy (INH, rifampicin, ethambutol, or pyrazinamide). By utilizing the images, the effects of the remaining growth plate cartilage on chronological changes of kyphosis after the initiation of chemotherapy were analyzed. The first assessment at postchemotherapy was at 1 year and at the final discharge time from the follow-up.

**Results:** Complete disk destruction at the initial examination was observed in 2 (5.0%) out of 40 cervical spine, 8 (26.7%) out of 30 dorsal spine, and 6 (19.4%) out of 31 lumbosacral spine. In those cases, kyphosis developed inevitably. In the remainders, the disks were partially preserved or remained intact. Among 101 children, initial kyphosis was maintained in 20 (19.8%), while kyphosis decreased in 14 (13.7%) children, and increased in 67 (66.3%) children with nonrecoverably damaged growth plate.

**Conclusion:** It was possible to predict the fate of the kyphosis at the time of initial treatment, but its predictive accuracy was low. Therefore, finally, it is recommended to be done at the end of chemotherapy. In children, the kyphotic deformity assessment should be continued till the maturity


**Keywords:** Chemotherapy, Children, Kyphosis, Spine, Tuberculosis.

**How to cite this article:** Moon M-S. Conservatively Treated Spinal Tuberculosis in Children: Ambulatory Chemotherapy. J Spinal Surg 2018;5(1):10-17.

**Source of support**: Nil

**Conflict of interest**: None

Surgeon

Department of Orthopedic Surgery and Traumatology, Cheju Halla General Hospital, Jeju Province, Republic of Korea

**Corresponding Author:** Myung-Sang Moon, Surgeon Department of Orthopedic Surgery and Traumatology, Cheju Halla General Hospital, Jeju Province, Republic of Korea, Phone: +8227855387, e-mail: msmoonos@hotmail.com

## INTRODUCTION

There are numerous previously published papers on spinal tuberculosis, mostly from the tuberculosis prevalent countries, such as India, Northern-Africa, Hong Kong, and Korea in the past.[1-16] Good-quality and informative papers are still being published from India.[9,10,15,16] However, pediatric spinal tuberculosis was less dealt in comparison with the adult tuberculosis, and those authors rarely focused on the effect of disk damage on the affected vertebral growth and kyphotic change.[1,2,5,12-16]

Children are different from adults in many aspects. A child has a growth potential in the growth plate, and high modeling capacity. Therefore, the kyphosis management of the pediatric spinal tuberculosis must be different from the adult.

Rajasekaran[9,10] reported the very informative natural course of the pediatric spinal tuberculosis in the late 1980. However, they did not discuss the role of the growth cartilage in the lesion which contributed to the column growth.

Based on the afore-mentioned information, the current authors designed this retrospective study, utilizing all their previously collected medical records, X-ray, and magnetic resonance imaging (MRI) data.

## MATERIALS AND METHODS

Consecutively treated 101 children with various stages of tuberculous disease processes, aged from 2 to 15 years, underwent this study. They were treated at 8 University hospitals and 3 general hospitals during the period 1997 to 2010, and were treated only with the combined antituberculous chemotherapeutics.

Forty (39.6%) children had the cervical and cervicodorsal junction lesions, 30 (29.7%) in the dorsal, and 31 (30.7%) in the lumbar and lumbosacral spines. Twenty-six (25.7%) children were under the age of 5 years, 43 (42.5%) with age range from 6 to 10 years, and 32 (31.6%) over 10 years of age. Eighteen (17.8%) children were partially paralytic; 3 in Frankel B, 12 in Frankel C, and 5 in Frankel D.

### Diagnostic Methods

Initial clinical diagnosis was made based on the disease history, complaints, and the physical findings which were augmented later by laboratory and image data, and

finally was reconfirmed by the physical response against chemotherapeutics.

For image diagnosis, simple radiograms and MRI were used. The MRI demonstrated more accurately the disk sparing. Thus, great emphasis was placed on the assessment of disk conditions including growth cartilage which was closely related to the regrowth and remodeling of the bony vertebra. This issue was one of the key points.

### Assessment of the Disease Arrest and Heal, and Stability of the Diseased Segment(s)

The keys in the assessment were images which were augmented by the clinical symptoms improvement and laboratory data.

Disease arrest point is the progress stop time on images in which no further vertebral damage occurs in conjunction with the normalized laboratory data. Disease heal (cure) point is defined when the image and laboratory data of the arrest point are maintained in addition to the radiographic findings, such as bony reformation, modeling, and intercorporal fusion. Diseased segment stability is defined when the same image findings of the arrest point are seen irrespective of corporal fusion.

### Assessment of Disk Condition at the Lesion Site and Rate of Spontaneous Fusion of the Diseased Segments

The disk space becomes narrowed when any part of its component structure is destroyed. Therefore, the assessment of disk space on simple radiographs and MRI is important, and more important is the assessment of the end-plate condition, whether it is irregular, disrupted, and has disappeared. Vertebral growth and shape modeling depend on the growth cartilage. In the case of complete disk disappearance, vertebral regrowth and modeling cannot be anticipated, while the regrowth is possible when the growth cartilage is preserved in spite of some disk space narrowing.

### Assessment of Changes of Kyphotic Deformity

The kyphosis is measured by Cobb angle, utilizing the simple radiograms during chemotherapy: Initiation, arrest, and cure points. Thereafter, the kyphotic change was measured with certain interval in the cases with the decreased and increased kyphosis. The effect of the spontaneously fused bloc vertebrae on kyphosis progress was also assessed.

### Assessment of the Diseased Segment Stability at the Time Points of Arrest and Cure

When there was the rapid progress of kyphosis at the fused and unfused arrested and healed vertebral lesion site, the segment was defined unstable. For such a case, a careful observation was carried out.

### Treatment Protocol

For all children, high-calorie protein diet was prescribed when they were hospitalized. However, it was impossible to check it after discharge.

For all children, directly observed chemotherapy was practiced under the children's parents' and their family members' supervision.

In all children, a 3-drug regimen was adopted: INH (H), streptomycin (S), and PAS (Pa) for 18 months [(3HSPa), 15HPa] was used between 1971 and 1975. Since 1976, 3 drugs, isoniazid (H), rifampicin (R), ethambutol (E), or pyrazinamide (Z), for 12 months (12 RHE or 12 RHZ) was adopted.

Supplementary immobilization was adopted. Head halter was routinely applied in all cervical cases for 7 to 10 days before definite therapeutic protocol was finalized. Before 1980, Minerva cast in 14 children was applied for 3 months because of the noted cervical instability. Thereafter, four-post cervical brace was applied in 7 children, and halo-shoulder apparatus for 4 months in 12 children. Seven children had no supporting apparatus.

## RESULTS

### Laboratory Data

Hematologic findings: Erythrocyte sedimentation rate at the initial examination was 41 mm/hour (31–54 mm/hour) and 14 mm/hour (9–17 mm/hour) at the post-chemotherapy 3 months.

C-reactive protein (CRP): average CRP at pre- and post-chemotherapy 3, 6, 9, and 12 months was 3.9 (2.3–4.7), 0.5 (0.23–1.4), 0.05 (0.04–0.16), 0.06 (0.03–0.13), and 0.03 mg/dL (0.01–0.09 mg/dL).

### Disk Conditions

On images, complete disk destruction was noted in 2 (5.0%) out of 40 cervical tuberculosis, 8 (26.7%) out of 30 dorsal tuberculosis, 6 (19.4%) out of 31 lumbar and lumbosacral tuberculosis.

All 16 (15.0%) children with complete disk destruction were the advanced cases at the initial diagnosis and chemotherapy.

### Disease Arrest and Cure, and the Diseased Segment Stability

In some cases, slow drug response was observed in the early stage of drug therapy, but finally, it did not influence the final cure. There was no nonresponder.

Spontaneous fusion occurred in 5 (12.5%) out of 40 cervical cases, 7 (23.3%) out of 30 dorsal and 4 (12.9%) out of 31 lumbar and lumbosacral cases at the end of chemotherapy.

In all, the disease arrest sign was observed at the average postchemotherapy 3 months (2.5–4.3 months), and cure was obtained at postchemotherapy 12 months; All the radiological and laboratory findings of the arrest point were maintained without further change till the cure. Additionally, signs of reformation of destroyed bone were observed.

The stability of the diseased segment was maintained till the cure point irrespective of intercorporal fusion status.

## Kyphotic Curve during Chemotherapy and afterward

Cervical tuberculosis (n: 40 cases): Among 40 children with cervical lesion, average initial 10° kyphotic angle was maintained in 8 (20%) children without change, and average 8° kyphosis decreased to 3° in 6 (15%) at the end of treatment. In 26 (65%) children, the initial 8° kyphosis increased to 16° at the cure time (Table 1 and Figs 1 and 2).

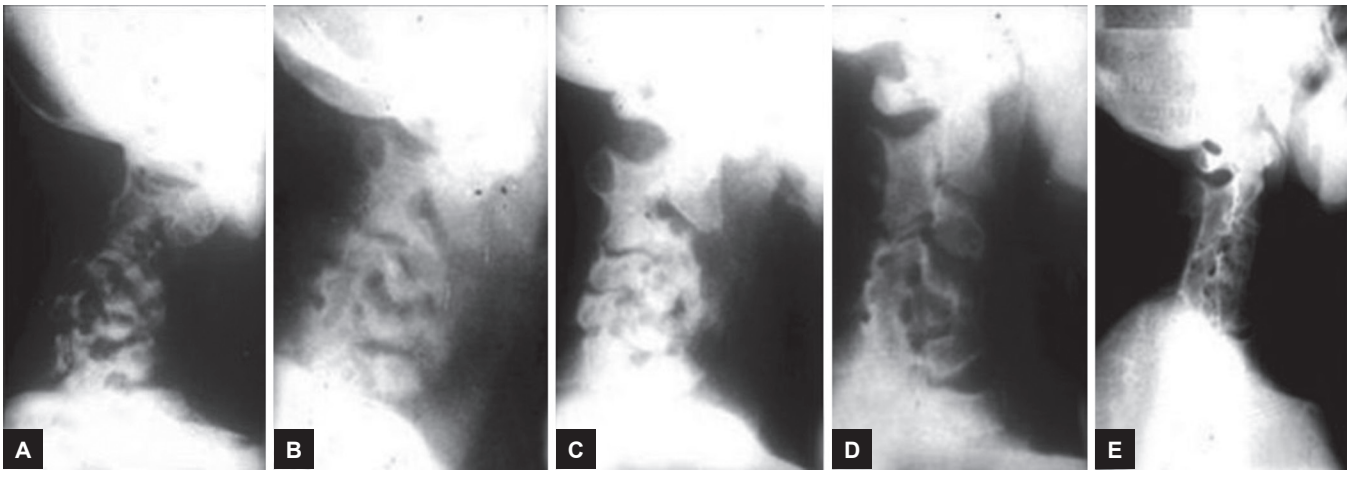
Dorsal tuberculosis (n: 30 cases): The initial 13° kyphosis was maintained till the end of treatment in 7 (23.3%), and in 4 (13.3%) children, average initial 15° kyphosis decreased to 10° at the end. In 19 (63.3%) children, the average initial 11° kyphosis increased to 23° at the end (Figs 3 and 4).

Lumbar and lumbosacral tuberculosis (n: 31 cases): In 5 (16.2%) children, the average initial 5° kyphosis was well maintained till the end of chemotherapy, and in 4 (12.9%), the average initial 12° kyphosis decreased to 4° at the end. In 22 (70.9%) children, the average 14° initial kyphosis increased to 25° at the end (Fig. 5).

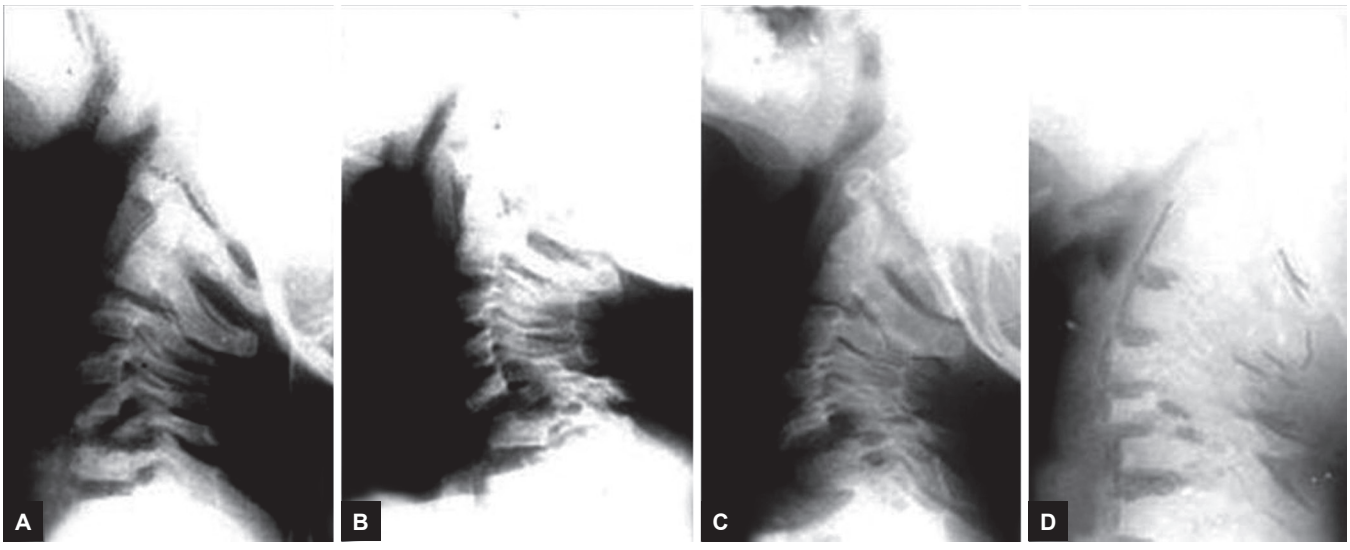
In summary, among the 101 children, 20 (19.8%) children could maintain the initial kyphosis. The initial

**Table 1:** Changes of tuberculosis kyphosis in each regional level (n: 101 children)

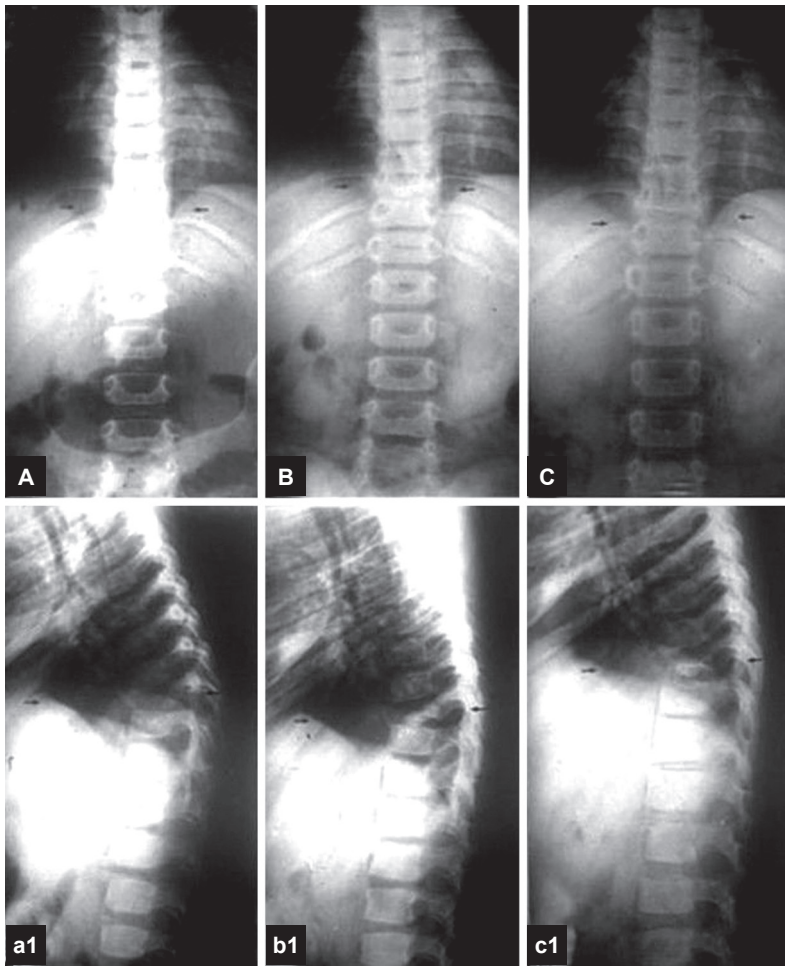
| | *Sagittal curve changes (kyphosis)* | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Spine levels* | *Initial* | *3M* | *6M* | *12M* | *18M* | *24M* | *36M (Final)* | *Difference* | *Remarks* |
| Cervical (n: 40) | | | | | | | | | |
| Unchanged (n: 8) | 10° | 10° | 10° | 10° | 10° | 10° | 10° | 0° | |
| Decreased (n: 6) | 8° | 8° | 5° | 5° | 3° | 3° | 3° | 5° | |
| Increased (n: 26) | 8° | 11° | 13° | 15° | 16° | 16° | 16° | 8° | |
| Dorsal and dorsolumbar (n: 30) | | | | | | | | | |
| Unchanged (n: 7) | 13° | 13° | 13° | 13° | 13° | 13° | 13° | 0° | |
| Decreased (n: 4) | 15° | 13° | 12° | 11° | 10° | 10° | 10° | 5° | |
| Increased (n: 19) | 14° | 18° | 21° | 23° | 23° | 23° | 23° | 9° | |
| Lumbar and lumbosacral (n: 31) | | | | | | | | | |
| Unchanged (n: 5) | 5° | 5° | 5° | 5° | 5° | 5° | 5° | 0° | |
| Decreased (n: 4) | 12° | 12° | 8° | 6° | 5° | 5° | 4° | 8° | |
| Increased (n: 22) | 14° | 18° | 23° | 26° | 28° | 28° | 28° | 14° | |



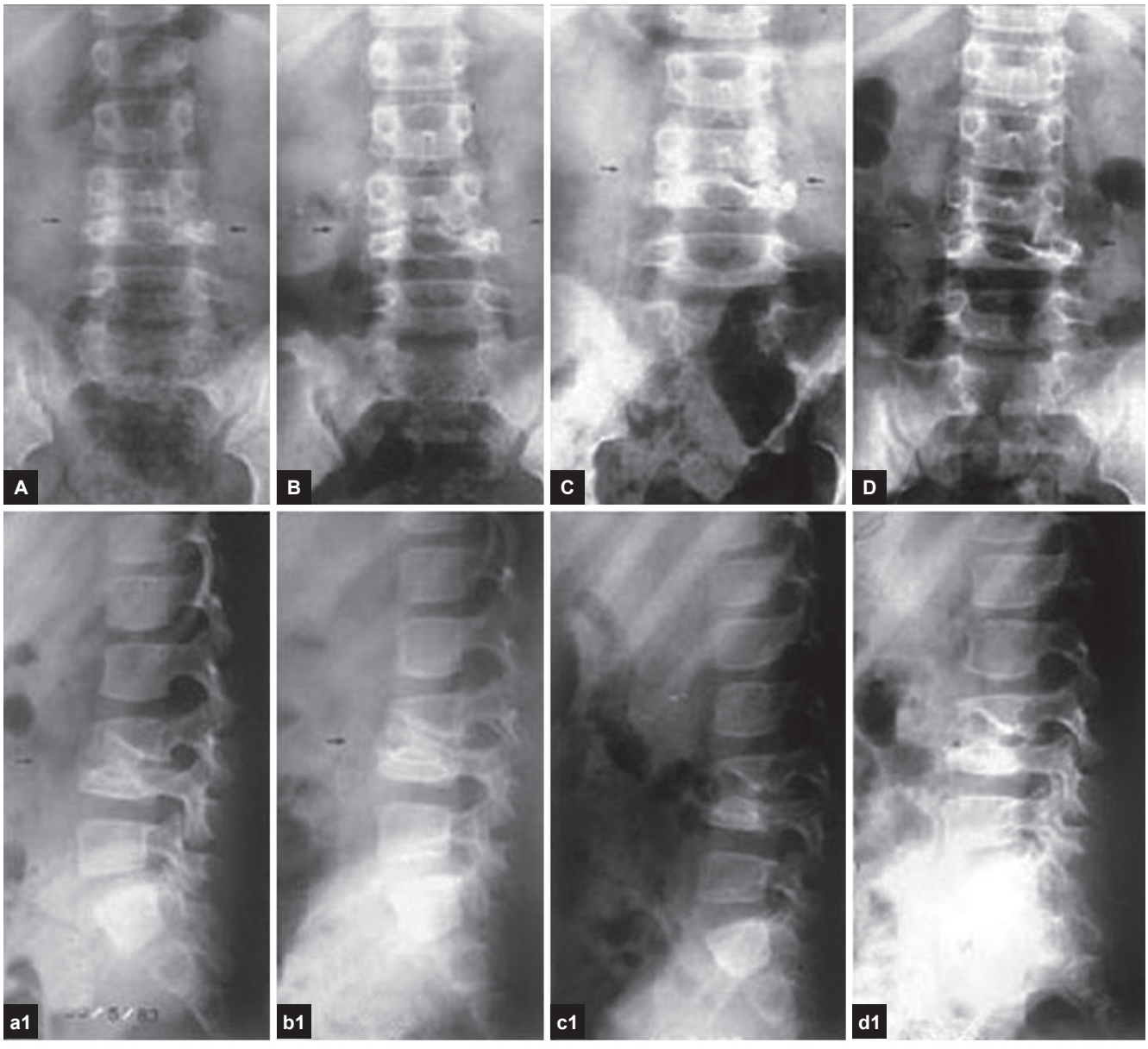

**Figs 1A to E:** Tuberculosis of $C_{3-6}$ in a 5-year-old boy. (A) Initial lateral radiograph showing narrowed disk spaces of $C_{3-4}$, $C_{4-5}$, and $C_{5-6}$ with round cervical kyphosis and huge prevertebral soft tissue shadow. Initially, cervical traction was applied in bed for 3 weeks under the cover of the triple chemotherapy which was followed by Minerva cast for 5 weeks. Radiograms taken at postchemotherapy, (B) 18 months, and (C) 36 months are shown in which we can observe the gradual spontaneous correction of kyphosis, visible undestroyed affected disks, and reformation of the diseased vertebral bodies. Radiograms, taken at 4 and 20 years (D, E) after initial chemotherapy, showing the fused $C_2$-$C_6$ block vertebra circumferentially with good spontaneous correction of kyphosis




**Figs 2A to D:** Tuberculosis of cervical spine at $C_5$-$C_7$ in a 2-year-old paraplegic boy, treated by triple antituberculous chemotherapy (INH, rifampicin, and ethambutol) for 12 months. Serial lateral radiograms taken at initial (A), 12 (B), 24 (C), and 36 (D) months are shown. (A) The initial radiogram shows the almost completely destroyed C6 body with minimum kyphosis. After chemotherapy, there was no further vertebral body destruction, while slippage of $C_5$ over $C_7$ occurred due to facet joint gapping at 12 months (B). However, anterior $C_5$ slippage was well reduced and stabilized spontaneously at 24 and 36 months (C, D)




**Figs 3A to C:** Tuberculosis of thoracic spine at $D_9$-$D_{11}$ in a 5-year-old boy; arrows indicate the lesion. Initial radiograms (A) show the flattened $D_{10}$ vertebral body with mild kyphosis (Cobb angle 18°), and the disease arrest. Gradual correction of kyphosis (Cobb's angle 10°) is seen at 12 (B) and 18 (C) months after triple chemotherapy. Intercorporal fusion did not occur




**Figs 4A to D:** Tuberculosis of $L_3$-$L_4$ in a 7-year-old boy, treated conservatively with triple chemotherapy for 12 months. On initial radiograms, incompletely fused $L_3$-$L_4$ bodies with cystic lesion in anteroinferior part of $L_3$ body (A) which was maintained until the last follow-up (B, C, and D). The flattened lumbar curve is seen

kyphosis decreased in 14 (13.7%) children, while the initial kyphosis increased in 67 (66.3%) children.

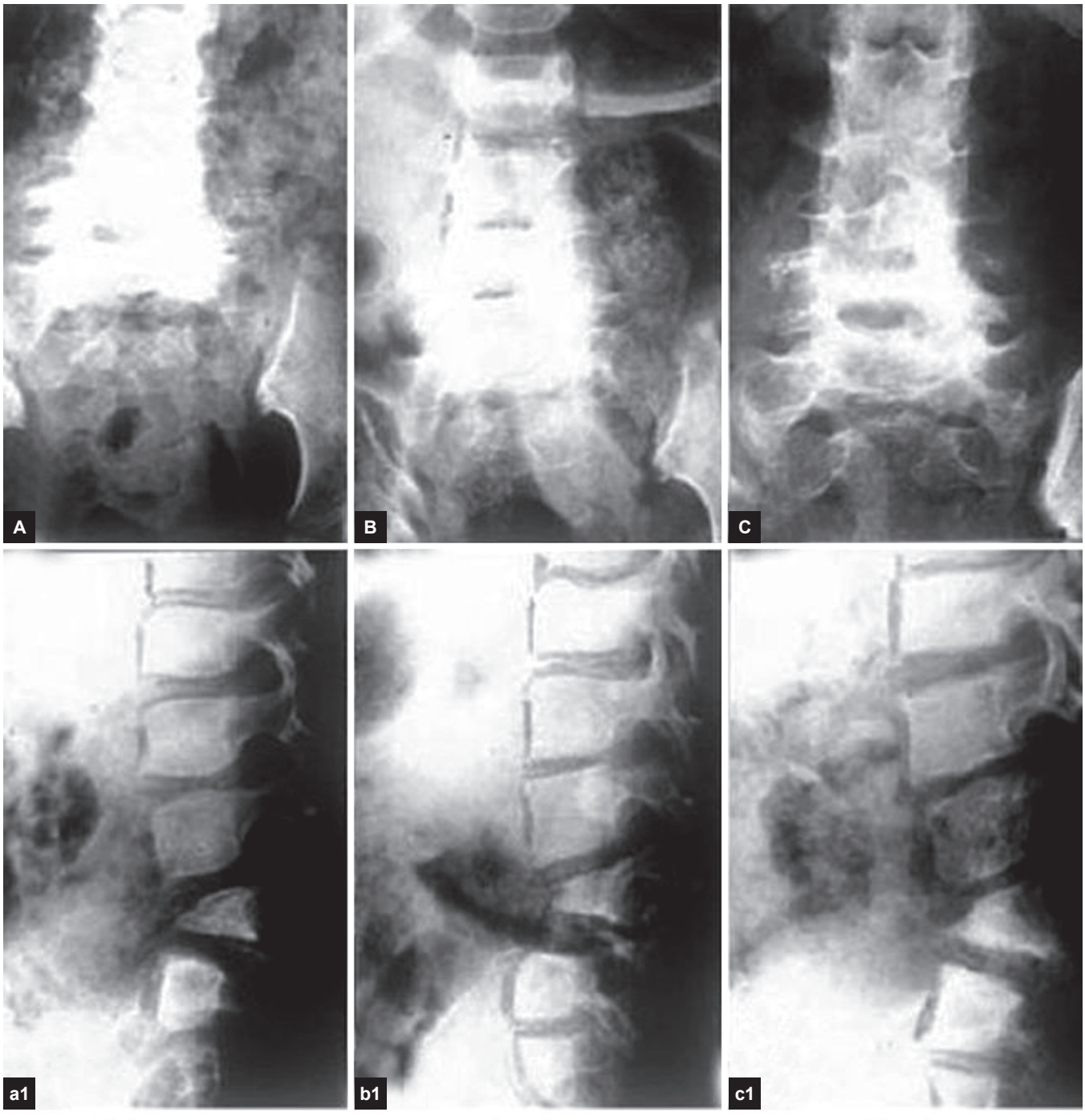
This fact evidently suggested that the initial growth plate damage in the advanced spinal tuberculosis hastened the progress of kyphosis, which is an inevitable complication during and after treatment (Table 1).

The main cause of the progressive kyphosis was the single-wedged fused bloc or unfused two-wedged vertebrae. Nonfusion was not the main cause of the progressive kyphosis.

## DISCUSSION

The primary objective of the management of the pediatric spinal tuberculosis is not only to cure disease but also to minimize the disease-related complications, such as kyphosis. The management of spinal tuberculosis aims at the prevention of destruction of the infected spinal column maximally, protection of the spinal cord and nerves, hastening the recovery of paralysis, and maintenance of the stability of the diseased segment.[2,3,5-8,11] None of the imaging modalities could solely provide the definite healing points, though all the available measures were mobilized.

All children in the current series presented different disease stages at the initial examination. The selection of the type of management was important.[11] Surgery should be applied only for the complicated tuberculosis. Physicians should assess the growth plate condition in




**Figs 5A to C:** Tuberculosis of $L_3$-$L_5$ (initial Cobb angle, 25°) in a 7-year-old girl, treated with triple chemotherapy for 12 months (A, A1). Retrolisthesis of wedged $L_4$ with increased kyphosis (final Cobb angle, 35°) is seen, though the disease healed (B, B1, C, C1)

the lesion before surgery through the image studies. MRI demonstrated disk sparing and the severity of vertebral destruction. MRI-based observation was the best method for disease assessment. The healing status was defined generally based on the combined clinical and radiological parameters, but improvement on image lagged approximately 3 months behind the clinical improvement in most of the senior author's previous studies.[2,3,11]

Until now, there have been controversies regarding the duration of antituberculous treatment (ATT) because each individual responded differently to ATT even under the same drug formula. Thus, it was needed to evaluate the spinal lesions clinically, hematologically, radiologically, and with contrast MRI to document the healing of the lesion after 8 months of ATT and subsequently to decide for the continuation or stoppage of treatment. The current authors did the same practice.

When surgery is indicated, gentle, less aggressive debridement of the lesion is the choice to preserve the remaining growth cartilage.[11]

Prediction of kyphotic change could be possible at the time of initial chemotherapy, but its predictive accuracy was rather low. The change of the kyphosis was primarily not directly related to the drug efficacy, and was rather related to the severity of the growth plate damage at the time of initial chemotherapy.

It is acceptable to stop the continuous observation in the noncurve progress form at the end of chemotherapy. However, in the other two forms, follow-up should be continued till deformity fixation.

The diseased corporal foci healed in two patterns: fusion and nonfusion. In either case of the current series, the healed original foci did not show sign of instability. As regards the stability of the healed focus, most surgeons were anxious whether the spinal stability could be obtained permanently or not. However, in the current authors' series, the stability of the healed diseased segment was well maintained even in the unfused cases.

As regards the growth of the fused pediatric bloc vertebral, the British MRC and Schulitz et al reported that in the pediatric spine, there may be progressive kyphosis despite a solid fusion because the continuing growth in the posterior spinal element may create further deformity, and that the anterior fusion alone had the worst prognosis in terms of progressive kyphosis.[1,13] On the contrary, Upadhyay et al[14] showed that a short anterior spinal arthrodesis done at an early age was not associated with the progress of deformity during growth and development from the disproportionate posterior spinal growth. Therefore, they did not recommend a posterior fusion to stop the posterior growth. The current authors supported the former one.[11]

The spontaneously fused bloc vertebra during and after chemotherapy becomes stable, but it is not a good news. There may be a possible progressive kyphosis due to continuing posterior element growth and may create further deformity. The spontaneous intercorporal fusion rate during chemotherapy in children is less than 15%, and 85% did not fuse. Thus, it is important to observe the influence of the healed unfused segment on kyphosis. If there is a rapid progress of kyphosis which exceeds over 50 to 60°, it should not be allowed because in those cases, the late unrecoverable paralysis develops gradually.[15-18] Those cases with rapidly progressive deformity and unacceptable deformity at the end of chemotherapy need not only the preventive surgery, but also corrective surgery should be carried out.

However, we should keep in mind that the undamaged growth disk cartilage in the lesion participates not only in the repairing of the destroyed bony vertebra, but also in the modeling of the spinal column.

In all the current children, spinal tuberculosis healed without any drug-related complications in spite of the kyphosis progression even after cure in 67 children (66.3%). However, this high percentile incidence of residual kyphosis was unrelated to the chemotherapy, and was primarily the end-product of the lately discovered advanced disease and treatment delay.

Based on the current study results, the early management is stressed under early recognition of the disease by the patients and the healthcare service personnel. Those are the keys not only for the cure of the disease, but also for the reduction of the disease-related crippling.

Lastly, it is stressed that medicine is the basic curative agent, and that surgery is only the adjuvant therapeutic means for the complicated conditions. Also, a continuous vigilant observation is recommended till growth maturity in children, particularly those who present the evidence of deformity progression.

## REFERENCES


1. Schulitz KP, Kothe R, Leong JC, Wehling P. Growth changes of solidly fused kyphotic bloc after surgery for tuberculosis. Comparison of four procedures. Spine (Phila Pa 1976) 1997 May;22(10):1150-1155.
2. Moon MS, Kim I, Woo YK, Park YO. Conservative treatment of tuberculosis of the thoracic and lumbar spine in adults and children. Int Orthop 1987;11(4):315-322.
3. Moon MS. Tuberculosis of spine. Controversies and a new challenge. Spine 1997 Aug;22(15):1791-1797.
4. A 10-year assessment of controlled trials of inpatient and outpatient treatment and of plaster-of-Paris jackets for tuberculosis of the spine in children on standard chemotherapy. Studies in Masan and Pusan, Korea. Ninth report of the Medical Research Council Working Party on Tuberculosis of the Spine. J Bone Joint Surg Br 1985 Jan;67(1):103-110.
5. Moon MS, Moon YW, Moon JL, Kim SS, Sun DH. Conservative treatment of tuberculosis of the lumbar and lumbosacral spine. Clin Orthop Relat Res 2002 May;(398):46-49.
6. Moon MS, Moon JL, Kim SS, Moon YW. Treatment of tuberculosis of the cervical spine: operative versus nonoperative. Clin Orthop Relat Res 2007 Jul;460:67-77.
7. Moon MS, Lee BJ, Kim SS, Lim SF. Evolution of management of spinal deformity: controversial issues and current concept review. J Spinal Surg 2010;2:295-305.
8. Moon MS, Kim JM. The effect of mechanical forces on vertebral growth. J Western Pacif Orthop Assoc 1974;11:1-16.
9. Rajasekaran S. The problem of deformity in spinal tuberculosis. Clin Orthop Relat Res 2002 May;(398):85-92.
10. Rajasekaran S. The natural history of post-tubercular kyphosis in children. Radiological signs which predict late increase in deformity. J Bone Joint Surg Br 2001 Sep;83(7):954-962.
11. Moon MS, Kim SS, Lee BJ, Moon JL. Spinal tuberculosis in children: retrospective analysis of 124 patients. Indian J Orthop 2012 Mar-Apr;46(2):150-158.
12. Bailey J, Gabriel M, Hodgson AR, Shin JS. Tuberculosis of the spine in children. Operative findings and results in one hundred consecutive patients treated by removal of

the lesion and anterior grafting. J Bone Joint Surg Am 1972 Dec;54(8):1633-1657.

13. Five-year assessments of controlled trials of ambulatory treatment, debridement and anterior spinal fusion in the management of tuberculosis of the spine. Studies in Bulawayo (Rhodesia) and in Hong Kong. Sixth report of the Medical Research Council Working Party on Tuberculosis of the Spine. J Bone Joint Surg Br 1978 May;60-B(2):163-177.
14. Upadhyay SS, Saji MJ, Sell P, Sell B, Hsu LC. Spinal deformity after childhood surgery for tuberculosis of the spine. A comparison of radical surgery and debridement. J Bone Joint Surg Br 1994 Jan;76(1):91-98.
15. Tuli SM. Tuberculosis of the skeletal system: bones, joints, spine and bursal sheaths, 3rd ed. New Delhi: Jaypee Brothers Publishers; 2004.
16. Jain AK, Aggarwal PK, Arora A, Singh S. Behaviour of the kyphotic angle in spinal tuberculosis. Internat Orthop (SICOT) 2004 Apr;28:110-114.
17. Masini M, Maranho V. Experimental determination of the effect of progressive sharp-angle spinal deformity on the spinal cord. Eur Spine J 1997;6(2):89-92.
18. Moon MS, Kim SS, Sihn JC. Tuberculous kyphosis—evolving concepts in prevention and treatment. J Musculoskeletal Res 2015 Sep;18(3):1-14.