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Management of Pierre Robin Sequence using Mandibular Distraction Osteogenesis with Long Term Follow Up

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Abstract

Pierre Robin described a congenital condition now known as Pierre Robin Sequence (PRS). The main features of this condition include micrognathia, glossoptosis and airway obstruction. Cleft palate is seen in PRS, however it is not considered a perquisite for the diagnosis. Glossoptosis and the compromised airway leads to feeding difficulties, failure to thrive and cardiac failure. Therefore, it is crucial to manage this condition as early as possible. Treatment options are variable and range from conservative measures to invasive surgical procedures such as mandibular distraction osteogenesis (DO)which is widely used. Each patient should undergo a proper diagnosis and assessment in order to select the suitable treatment plan. We report our experience with PRS patients, their management using DO we also report the variety of complications we have encountered while treating these patients.

Keywords: Pierre Robin; Micrognathia; Glossoptosis; Airway Obstruction; Distraction Osteogenesis

Introduction

In 1923 Pierre Robin described a congenital condition characterized by glossoptosis and micrognathia leading to upper airway obstruction with breathing difficulties [1] it was considered to be a syndrome but is now known as Pierre Robin Sequence(PRS). The sequence starts with a mandibular hypoplasia in utero which then displaces the tongue posterior and superior, this prevents the palatal shelves from fusion leading to the classic features of micrognathia, glossoptosis and the cleft palate [2] leading to tongue base obstruction and respiratory distress [3]. The cleft palate has been associated with (PRS) however, it is not considered a perquisite for the diagnosis and it usually appears as a wide U shaped cleft soft palate when present [2]. PRS can occur isolated or associated with a syndrome, such as Stickler, velocardiofacial, craniofacial microsomia and treacher Collins [4].

The resulting compromised airway varies is severity from mild, moderate to severe airway obstruction. This can lead to feeding difficulties, failure to thrive, growth retardation. In severe cases the airway obstruction can lead to core pulmonale due to respiratory failure leading to right sided heart failure [5]. Therefore, it is crucial to manage this airway problem as early as possible.

There are numerous potential treatment options. They range from conservative non-surgical interventions to invasive surgical procedures. The selection of the appropriate approach depends on the cause of the apnea and the severity of the condition. There is an agreement that patients with a mild compromised airway may benefit from simple positional therapy in prone or lateral position with or without the administration of positive airway pressure.70% of PRS patients will respond to positional therapy [6]. There is also an agreement that tracheostomy is best reserved for severe cases with subglottic obstructions from laryngomalacia, tracheomalacia and in patients with central apnea [7-9]. However, tracheostomy is best avoided as it has been noted that only 10% of PRS will need it [6]. Reports regarding the management of the remaining 20% of PRS patients with variable presentation are controversial and they include a set of non-surgical and surgical methods like glossopexy, mandibular traction, floor of mouth subperiosteal release, mandibular distraction osteogenesis and tracheostomy [2].

In 1992, the introduction of mandibular distraction osteogenesis by McCarthy., *et al*, as a means of correcting craniofacial abnormalities has opened a new window to treat this complex problem [10]. Dauria and Marsh have reported the benefits of bilateral mandibular distraction osteogenesis in managing patients with PRS [11]. Monasterio., *et al*, have also reported the successful use of mandibular distraction osteogenesis (MDO) to relief airway compromise in patients with PRS [12].

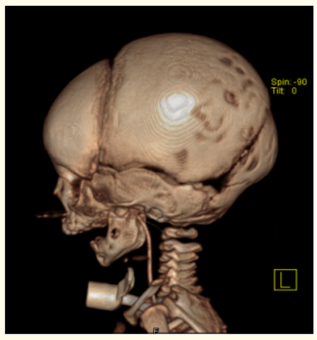
Guidelines for the type and timing of intervention in PRS are vaguely outlined in the literature. The aim of this article is to report our experience with patients diagnosed with PRS and their management to relief their compromised airway which included MDO. We also discuss the advantages and complications of this technique and our findings after a long term follow up.

Patients and methods

In this retrospective study we reviewed all patients diagnosed with PRS referred to the maxillofacial surgery unit at king Abdulaziz university hospital (KAAUH) between 2004 -2016 they were referred either from the neonatal intensive care unit (NICU) at KAAUH or from other hospitals. Patients referred from the NICU, Airway management was started by simply prone positioning then placing a nasopharyngeal airway or applying CPAP and intubation. Patients referred from other centers were either already on tracheostomy and nasogastric gavage or just showing deterioration in airway despite being discharged on conservative measures.

All patients referred from ICU underwent thorough clinical examination by a multidisciplinary team of neonatal ICU specialists, pediatric surgeons, pulmonogists, anesthetists and ENT surgeons. Upper airway evaluation included Laryngoscopy along with flexible fiberoptic broncoscopy, to evaluate tongue position and to rule out airway abnormalities like webs, tags or stenosis. A diagnosis of a compromised upper airway due to micrognathia and glossoptosis was confirmed. A CT was performed in some cases to assess the mandible and upper airway (Figure 1a and 1b) then a bilateral MDO was performed to advance mandible and improve upper airway.

Patients were operated upon under general anaesthesia either through the tracheostomy or by fiberoptic nasal intubation. Preoperative antibiotics were administered and bilateral submandibular incision were made. Bilateral corticotomies were created we applied the oblique corticotomy in the mandibular antigoneal region or the inverted L corticotomy. A reciprocating saw was used to perform the coricotomies. Before completion of the osteotomy with osteotomies, two pediatric internal mandibular distractors were fixed on each side. The distractor's activation arm was exposed through an incision either through the buccal mucosa then we modified the technique through a retromandibular skin incision. The submandibular incision was sutured in layers (Figure 1c-1e). The distractor was activated 1mm intraoperatively. After a latency period of 1 day for new-borns and 3 days for older infants. The distractor was activated at a rate of 2mm /day and a rhythm of twice /day.



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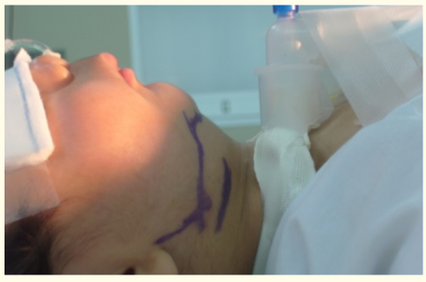
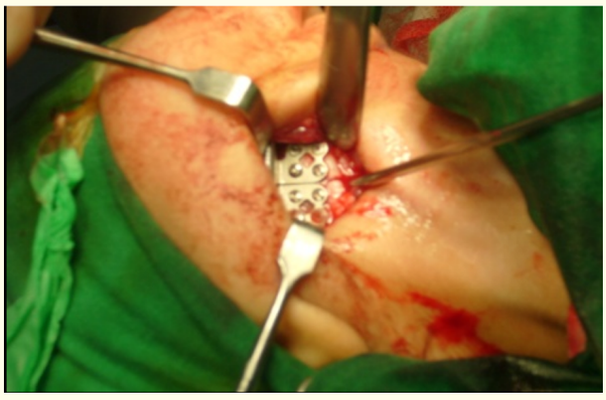


1b

Patients were operated upon under general anaesthesia either through the tracheostomy or by fiberoptic nasal intubation. Preoperative antibiotics were administered and bilateral submandibular incision were made. Bilateral corticotomies were created we applied the oblique corticotomy in the mandibular antigoneal region or the inverted L corticotomy. A reciprocating saw was used to perform the coricotomies. Before completion of the osteotomy with osteotomies, two pediatric internal mandibular distractors were fixed on each side. The distractor's activation arm was exposed through an incision either through the buccal mucosa then we modified the technique through a retromandibular skin incision. The submandibular incision was sutured in layers (Figure 1c-1e). The distractor was activated 1mm intraoperatively. After a latency period of 1 day for new-borns and 3 days for older infants. The distractor was activated at a rate of 2 mm /day and a rhythm of twice /day.



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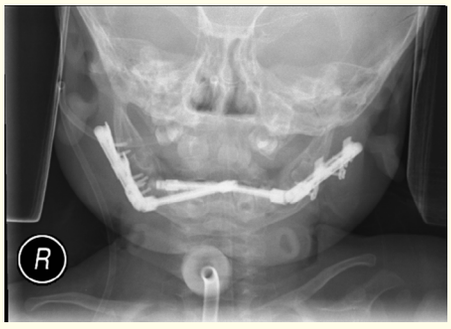


1d

1e

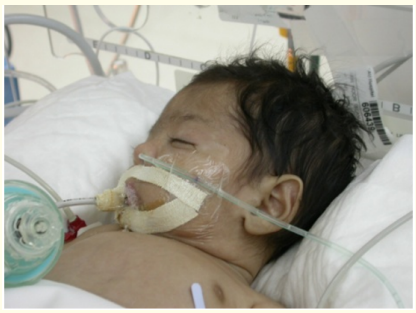
Figure 1: (a) 6-week-old male patient with pierre robin sequence and underwent tracheostomy and nasogastric tube placement at a different center 3D CT showed severe micrognathia. (b) Submandibular incision marking before performing bilateral mandibular distraction osteogenesis. (c) Fixation of mandibular distractor. (d) Posteroanterior radiograph showing bilateral mandibular distractors with mild dislodgement of the left distractor. (e) Clinical picture showing patient profile after four years follow up with good mandibular development.

Patients with tracheostomy were evaluated at the ENT clinic upon completion of the activation phase, in order to assess the airway progress after mandibular advancement. After a consolidation period of 8 -12 weeks, the distractors were removed under general anesthesia.

Results

18 Patients diagnosed with PRS presented with severe micrognathia compromising the airway. 10 females and 8 males. 11 patients diagnosed and referred from outside hospitals on tracheostomy. Four patients were referred from NICU, three on CPAP and one patient was intubated at birth. The rest of the patients were diagnosed at our outpatient clinic. Ages ranged between 1 day and 15 months old. All patients underwent bilateral mandibular distraction osteogenesis using internal pediatric mandibular distractors except one patient who responded to conservative treatment. Activation was started on the first postoperative day, at a rate of 2 mm per day. The consolidation period was 6 to 8 weeks. One patient intubated in NICU upon birth was successfully extubated on the 5th postoperative day after completing 10 mm distraction which improved the airway (Figure 2). 3 patients on CPAP in NICU were placed on nasal cannula and transferred to padiatric ward during the distraction phase due to improved airway. 11 patients on tracheostomy were reassessed at the ENT clinic upon completion of distraction phase before removal of distractors, for possibility of decannulation. Two patients were decannulated upon distractor removal and decannulation was delayed upon soft palate repair in 9 patients. Two patient required redistraction with soft palate repair after they underwent lip tongue adhesion during the first consolidation phase to augment the effect of distraction as the glossoptosis was still a problem. One patient developed bilateral temporomandibular joint ankylosis after undergoing bilateral mandibular distraction and required gap arthroplasty and costochondral reconstruction, followed by redistraction osteogenesis six months later, however reankylosis was noted with restricted mandibular growth (Figure 3). One patient was diagnosed with tracheomalacia during endoscopy performed during distractor removal as nasoendoscopy was not possible before mandibular distraction and decanulation was not possible. The follow up period varied between 2 and 10 years. We had two sets of identical twins. The first set where two females, however, only one of the twins was diagnosed with PRS however she responded well to conservative treatment and was followed up for three years showing no signs of airway compromise, however the micrognathia was still noted compared to her twin (Figure 4). In the second set of female twins, the both presented with micrognathia and compromised airway, however, one

responded well to conservative treatment while her sister required mandibular distraction osteogenesis. The follow up ranged from 2 - 10 years. Most patients showed satisfactory mandibular growth with airway improvement (Figures 1f, 2d).



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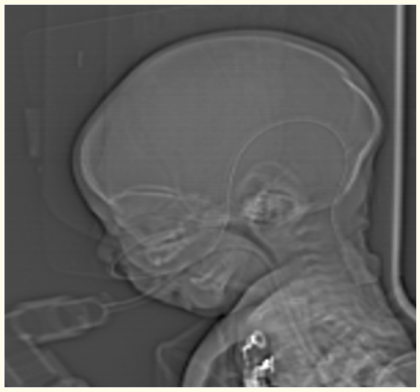

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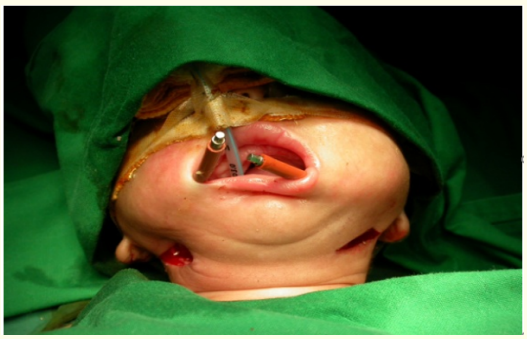

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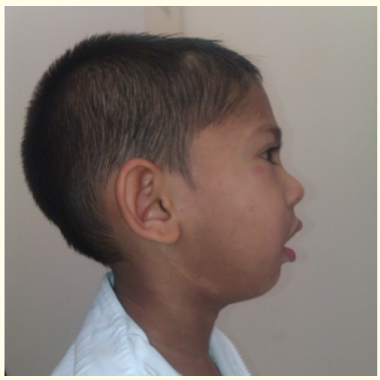
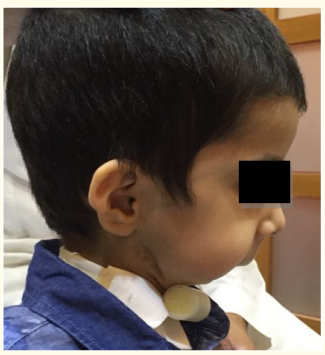


2d

Figure 2: Five days old male patient diagnosed with pierre robin sequence (micrognathia, cleft palate). (a) Endotracheal tube was inserted in NICU to manage the compromised airway. (b) Lateral cephalometric radiograph showing severe micrognathia and endotracheal tube in place. (c) Surgical placement of bilateral mandibular distractors. (d) Patient profile after four years follow up showing good mandibular development.



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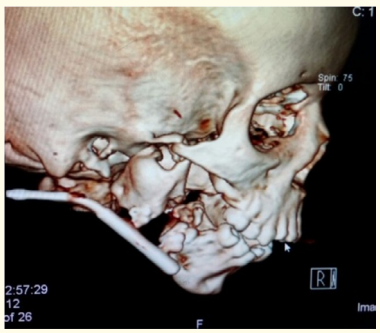

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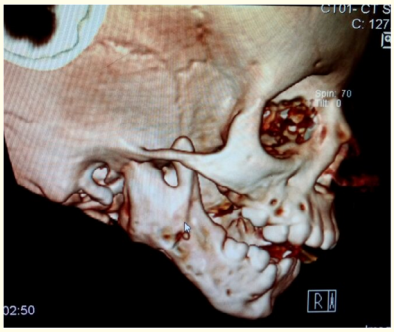

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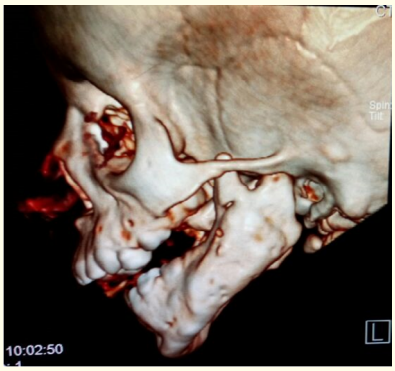

3d

Figure 3: (a) Clinical picure of two year old patient with tracheostomy developed bilateral TMJ ankylosis after bilateral mandibular distraction ostegenesis. (b)3D CT images of patient showing distractor in place during activation phase. (c) and (d) CT images showing bilateral TMJ ankylosis three weeks after removal of distactor.

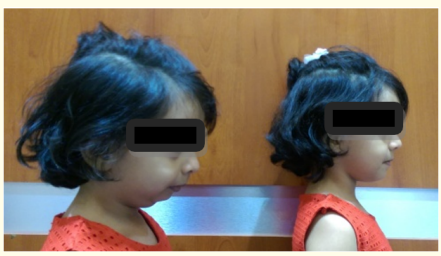

Figure 4: Identical twins, patient on the left presented with PRS at birth, conservative treatment was applied with close follow up.

Discussion

Patients with PRS are born with Micrognathia and glossoptosis thus leading to an airway obstruction. Management of neonates with airway obstruction remains to be a controversial challenge with very few published reports regarding the standard patient management and evaluation [13-15].

Though the aetiology of PRS is still controversial, defining the type of PRS will be the first step towards the most suitable management. PRS can be isolated or part of a syndrome, the latter usually shows a more severe form of compromised airway as we had observed in our two patients with stickler syndrome. As it has been noted in the literature that in such cases are genetically programmed to have a malformed retrognathic mandible [16]. PRS has also been reported in identical twins which supports the genetic impact for PRS [17]. We had two sets of twins, one identical and one non-identical. Non-identical twins with PRS supports the literature which hypothesized that mandible growth restriction can be caused by multigravid pregnancy which could place the fetus's chin in flexed position into the chest and restrict growth [16].

A proper evaluation of the airway is the next step in managing PRS patients this is done using radiographs and nasoendoscopy. Most PRS patients will show an obstruction at the base of tongue however some patients can have another obstruction beyond that level. If results show a clear airway, then central causes of this problem should be investigated. However, if the results show airway abnormalities causing infraglottic obstruction like, laryngomalacia or tracheomalacia, then a tracheostomy is considered as an initial management until a more definitive surgical intervention is applied. Test results for all our patients showed airway obstruction at the level of the tongue base due to micrognathia and glossoptosis except for one patient who presented with a mild laryngomalacia which resolved over time.

It has been noted that normal growth and craniofacial development may improve the airway within the first 4 to 6 months of age. However, there is a great deal of controversy regarding this matter and the infant will need some sort of intervention during those early months of his life. A number of therapeutic measures have been suggested in order to relief the upper airway obstruction in patients with mild forms of PRS. These include surgical and non-surgical interventions according to the severity

of the airway obstruction. Positional therapy and nasopharyngeal airway could be placed in for 2 to 4 months in order to maintain the airway. However, this treatment is mostly successful in nonsyndromic patients with micrognathia [18]. Other conservative non-surgical measures include positive airway pressure (CPAP) if tolerated and nasal stents using small diameter endotracheal tube. However, it must be noted that these measures are used in mild to moderate cases [11]. Most of our patients were started on a trial of non-surgical methods when referred from the same institution, however patients referred from outside hospitals were already on tracheostomy. So, they had been already been started on the surgical route.

If conservative measures fail in mild to moderate cases then surgical interventions are advocated. Predicting which patients will require surgical intervention and which will improve with conservative methods is still quite controversial. The surgical intervention is often based on clinical findings and some studies have developed a grading system with clinical criteria and algorithms, however it still remains subjective and incomplete. A multidisciplinary team has evaluated all our patients in order to select the appropriate route of treatment.

Surgical measures include; tongue lip adhesion (glossopexy), release of suprahyoid muscles and tracheostomy in severe cases. Each surgical technique has its advantages and draw backs. Tongue lip adhesion successfully relieves the airway obstruction in patients unresponsive to positioning methods however, it is considered to be a temporary solution for the airway until the catch-up mandibular growth takes place. It is also associated with complications including wound dehiscence [19] disturbed feeding and affection in the development of speech skills and sound production [20,21]. We used this technique on two of our patients after undergoing mandibular DO due to severe glossoptosis resulting in improved airway, however both patients required redistraction of the mandible.

Subperiosteal release of the floor of the mouth could be an option in some patients. This surgery is directed at the pathologic process involved in patients with PRS, that is, the abnormal tightness of the tongue musculature. However, it is considered an invasive procedure with few reported successful cases [22]. Mandibular traction is a surgical therapy that is a minimally invasive alternative with no serious complications such as scars or nerve damage, however it requires that the infant is kept intubated and kept still with a traction devise attached to the mandible for about two weeks [23].

In the most cases with severe airway obstructions and abnormalities beyond tongue base, tracheostomy seems to be the safest and most reliable surgical method especially in emergency situations. However, it carries many complications and side effects which include, tracheal stenosis, granulations, tracheomalacia, chronic bronchitis sudden death due to tube obstruction or dislodgement, and speech impairment [24,25]. Tracheostomy is usually used as a short-term solution to this complex problem. However, in severe cases the decision of whether to perform a tracheostomy or mandibular distraction osteogenesis depends the patient's condition and the available facilities and services. Thirteen of our patients underwent tracheostomy for management of their compromised airway at the referring center which is probably due to the lack of a specialised team in these centers to diagnose and manage such cases. So, a tracheostomy was their only choice in such cases.

The use of MDO to lengthen the mandible is the favourable technique in managing airway obstruction in patients with PRS. MDO has been applied successfully to improve the compromised airway in children with mandibular hypoplasia [26-28]. The ability to achieve the required large mandibular advancements along with simultaneous advancement of the tongue base makes distraction osteogenesis a highly attractive option. In addition, advantages of MDO include minimal relapse, no donor site morbidity, short operative time and fewer complications [29]. Earlier attempts to advance the mandible mechanically to relief airway obstruction in patients with micrognathia were abandoned despite the correct concept due to temporomandibular joint affection and ankylosis [28]. However, with MDO there is less damage to the TMJ due to less loading with gradual distraction. The surrounding soft tissues are gradually expanded as well. Although it has been argued that adaptation of the surrounding soft tissue envelope does not present a problem in infants due to its high elasticity. Distraction does not cause damage to TMJ, but it has been noted in previous studies that hypomobility is a common postoperative complication [30]. A study on condylar position before and after mandibular distraction osteogenesis in children with PRS noted outward movement of the condyle in horizontal direction; this movement may be among the causes of postoperative joint adhesions and joint rigidity following mandibular distraction osteogenesis [31]. One patient developed bilateral TMJ ankylosis after undergoing distraction osteogenesis which is a rare finding is, however one recently published article noted temporomandibular joint ankylosis after early mandibular distraction osteogenesis and questioned the possibility of that being a new syndrome [32]. Another feared complication is injury to the

inferior alveolar nerve or the developing tooth buds. This could be avoided by careful selection of the corticotomy site and applying the inverted L osteotomy which we converted to as this technique guaranteed dense bone and avoidance of tooth buds and tin bone [33], some reported the use of piezosurgery to minimise the risk of damage [34]. The development of an anterior open bite during the activation period is a common observation. We experienced this in two patients, however, the open bite resolved after removing the distractors. Multisector external distractors could be used to avoid this problem in addition to the use of curvilinear devices as reported in some cases [35].

Premature consolidation is another reported complication. This was managed by refracturing the segment and increasing the distraction rate. More inconvenient complications included distractor fracture and loosening of pins or screws. One case showed detachment of the screws in proximal segment of the distractor. This was probably due to the naturally soft rich cancellous structure of the infant mandible. This was managed by continuing to activate the intact side and the patient showed improved airway. Other reported complications include soft issue scarring and infection. External distractor pins leave a scar along their track, but the advantage is to spare the patients another surgical procedure for distractor removal. On the other hand, internal distractors as used in our patients have the advantage of a low profile and lack of external pin scaring, however it requires a second surgical procedure for removal and this is usually done through skin which may lead to scarring and fibrosis which may possibly lead to growth disturbance. The use of newly introduced resorbable distractors would eliminate the need for a second surgical procedure for removal and the associated complications [36].

We are living in the high-speed era and distraction osteogenesis is a lengthy procedure that requires 2-3 weeks of distraction followed by 12 weeks for consolidation. Some have proposed a rapid distraction protocol by administering bone morphogenic protein 2(rhBMP-2) in neonates with PRS [37]. This technique allows rapid mandibular advancement through distraction osteogenesis; however this does not always lead to rapid improvement of upper airway.

The predictors of success or failure after MDO are quite variable. Mild to moderate sleep apnea is common following MDO, however improvement was noted over time according to many large studies [38]. This was observed in some of our patients who needed a longer time to show improvement in airway after MDO and this should not be considered to be a failure. Another important point to consider is that the timing of decanulation in PRS patients with tracheostomy is quite variable with a median time of 97 months according to one study [39]. We observed a highly variable timing of decanulation among our patients, and it must be noted that the ability of MDO to expedite decanulation in PRS is still being debated. However, improvement in upper airway after MDO to allow earlier decanulation in non-syndromic PRS is non-debatable and has showed upper airway improvement in all of our patients.

Conclusion

The use of mandibular distraction osteogenesis is an effective measure in managing patients with Pierre Robin Sequence. We have reported our positive experience as noted by other studies , that mandibular distraction osteogenesis can be used to avoid tracheostomy in patients with a compromised airway due to micrognathia .It can also be used to decannulate patients with tracheostomy. However ,we have reported a long term follow up of 9 years after mandibular distraction without any observed adverse effects .The literature contains only a handful of reports with long term follow up after mandibular distraction osteogenesis in neonates and the idea of mandibular growth following DO is still not quite clear .This unclear issue can only be unveiled through long term follow up studies .This millennium might unleash the answer as the first neonates who have undergone DO reach skeletal maturity.

Conflict of Interest

No conflict of interest.

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