

## ORIGINAL ARTICLE

ANTHROPOMETRIC ASSESSMENT OF PAEDIATRIC FLAT FOOT:  
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**Background:** Flat-foot involves total collapse of medial longitudinal arch, which becomes distressful when children begin to stand on their feet. Flat foot is usually diagnosed on clinical examination, however due to lack of a standardized protocol, there are conflicting views regarding its management. The objective of this study is to determine the accuracy of radiographic and podometric measurements in diagnosing paediatric flat foot. **Methods:** It was a cross sectional diagnostic accuracy study. Eighty-four children of preschool and school going age were recruited equally into control and flat foot groups. Each child was examined clinically and was further classified into having flexible or rigid flat foot. For radiographic assessment, lateral and anteroposterior foot radiographs were taken while footprints were captured using podoscope and analysed with FREESTEP software. The diagnostic accuracy and correlation among different parameters were also computed. **Results:** Clinically, of the 42 children in the flat foot group, 26 had flexible while 16 had rigid flat foot. Of these, 40 children were flat footed on one or more radiographic parameters, while 36 had podometric measurements within the flat foot range. Radiography had the sensitivity and specificity of 95% and 69%, respectively, while podometry was 86% sensitive and 47% specific. Clark's angle had highest sensitivity of 90%, with AUC of 0.952. A strong positive correlation was found between arch index and talocalcaneal angle ( $r=0.805$ ). **Conclusion:** The diagnostic accuracy of radiography was more than podometry. More specific and sensitive parameters in combination with clinical assessment may prove to be useful in the management of paediatric flat foot.

**Keywords:** Flat foot; Flexible flat foot; Rigid flat foot; Podoscope; Foot arch; Sensitivity; Preschool children; School going children

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## INTRODUCTION

The adult human foot has been arranged in the form of arches for its optimal functioning and the foot posture maintained primarily by the contour of the medial longitudinal arch.<sup>1</sup> Here there is a noticeable raised margin between rounded part of big toe and the heel on the medial side of the foot forming the medial longitudinal arch. The arch on the lateral side of the foot is a bit flatter as compared to arch on the medial side of the foot.<sup>2</sup> Children on the other hand in their earlier years of life have predominantly flat feet. But this is basically due the fatty pad in their soles, undeveloped foot structures and different walking patterns. However, in some children this normal development of foot arches is hindered resulting in flattening of the arches and hence flat feet, which is one of the most common paediatric foot disorders in clinical practice.<sup>3</sup>

It has been estimated that almost 90% patients that report to clinics with foot disorders are that of flatfoot.<sup>4</sup> Due to a lack of a standardized criterion for flat foot diagnosis, its exact prevalence varies from population to population.<sup>5</sup> Literature suggests that the

prevalence of paediatric flat foot in pre-schoolers (2–6 years) is 21–57%. This prevalence decreases with increasing age and is reported around 13.4–27.6% in school going children<sup>6</sup> and only 4% in children of 10 years age<sup>7</sup>. This may be attributed to the developmental changes taking place in the foot arches.<sup>8</sup> The crucial age for the development of foot arches is 6 years<sup>9</sup> as they develop rapidly between the age of 2–6 years and fully develop by 12 years girls and 15 years in boys<sup>8</sup>. Based on the severity and symptoms of the disease, Harris and Beath, divided patients with flatfoot into 3 classes, i.e., rigid flat foot, flexible flat foot and flexible flat foot with short Achilles tendon.<sup>10</sup>

The patients with paediatric flatfoot may present with foot pain, discomfort and stress fractures<sup>11</sup> while many may remain asymptomatic<sup>10</sup>. Flexible flat foot is most common in the first 10 years of life during which foot arch disappears in weight bearing position and reappears on extension of great toe or with standing on toes. Symptoms of flexible flat foot include pain at medial side of mid foot and patients with rigid flat foot have pain in multiple areas of foot.<sup>12</sup> The rigid type of flat foot has

numerous causes and mostly progresses to painful foot conditions.<sup>13</sup>

The diagnosis of flat foot is mostly based on clinical examination. The foot with normal looking arch is classified as normal and the foot that does not possess a visible medial arch is classified as flat foot.<sup>14</sup> However, certain complicated cases of flat foot have also been reported due which several indirect diagnostic procedures such as foot print<sup>15</sup> and photographs analysis<sup>16</sup> and direct methods such as anthropometric and radiographic assessments have been used<sup>17</sup>. These methods incorporate the analysis of multiple parameters for definitive diagnosis of the flat foot. However due to the lack of expertise, these methods are not commonly used and so a standardized protocol is yet to be established. Further due to this deficiency and subjective nature of both these tools, there is always a margin of human error. Moreover, the precise classification and diagnosis of flat foot is very critical for an appropriate treatment plan.<sup>18</sup> This study was aimed at determining the diagnostic accuracy of the radiographic parameters versus the podometric parameters in diagnosing paediatric flat foot.

## MATERIAL AND METHODS

This study was approved by the Advanced Study and Research Board (ASRB) under: DIR/KMU-AS&RB/AA/000717 University ethical committee (DIR/KMU-EB/AA/000542). The patients and controls were recruited from PIPOS Peshawar and Orthopaedic Department DHQ hospital KDA Kohat for study duration of six months from March to September 2018.

In this study 84 children of preschool and school going age were recruited into two groups, the control group consisting of 42 children with normal feet morphology and a flat foot group comprising of 42 children with flat foot. Ages of these children ranged between 3–10 years. For flat foot group only freshly diagnosed cases of paediatric flat foot were included and asymptomatic with flexible flat foot having age  $\leq$  5 years, any other congenital anomaly or gait problems were excluded from the study. The sequence of events, which were followed for data collection, is mentioned in Figure-1.

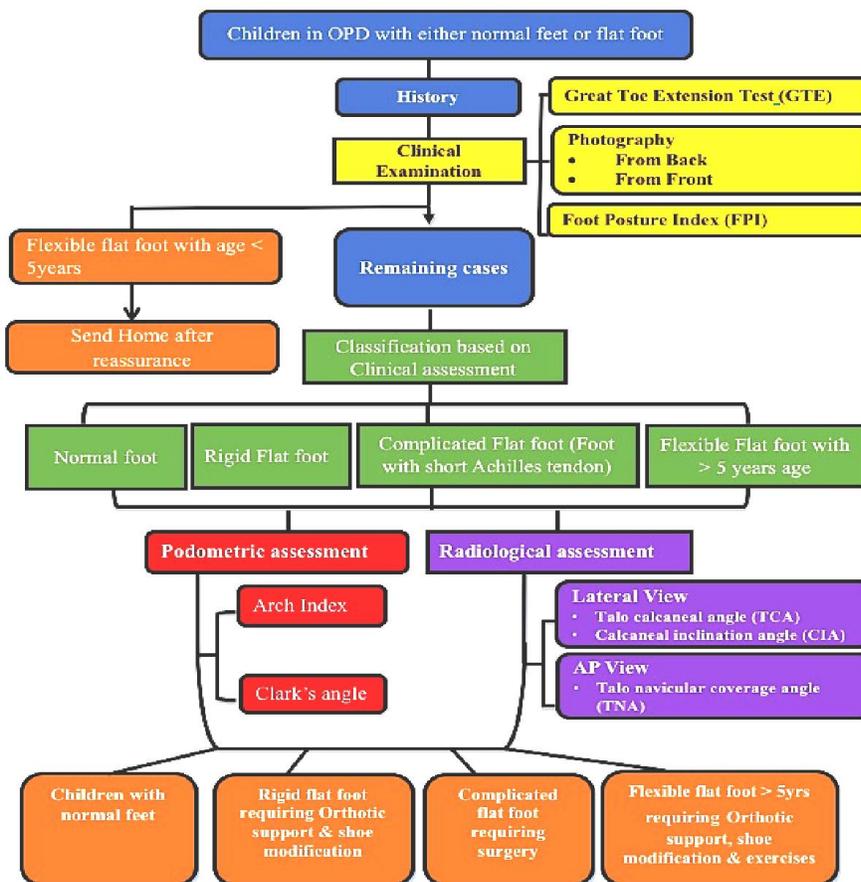


Figure-1: Sequence of events for data collection procedure

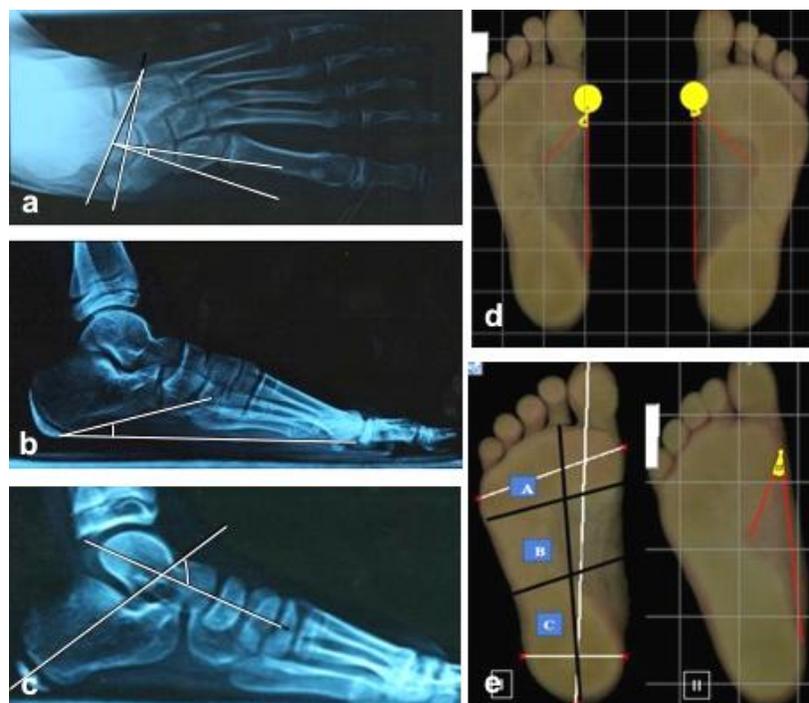
The clinical examination included great toe extension test (GTE), photographic assessment and foot posture index (FPI). The great toe extension test was performed with the patient bearing their own weight with the great toe dorsiflexed and observed for increasing convexity of the Arches of the foot. A positive result (arch formation) resulted from the flat foot being flexible. A negative result (lack of arch formation) was seen with rigid flatfoot. The photographs of the feet were taken from the front and the rear while the patient was in standing position.

The Foot posture index (FPI) was used to quantify the degree to which a foot is pronated or supinated.<sup>19</sup> The FPI is evaluated in standing children using six parameters as; 1) Talar head palpation, 2) Curvature at the lateral malleoli,, 3) Inversion/eversion of the calcaneus, 4) Talonavicular bulging,, 5) Congruence of the medial longitudinal arch, and 6) Abduction/adduction of the forefoot on the rare-foot. Each item is scored on a scale of -2, -1, 0, +1, +2 (0 for neutral, -2 for clear signs of supination, and +2 for clear signs of pronation), and all scores are summed. The final score ranges from -12 to +12; a larger positive value indicates a more pronated foot.<sup>20</sup>

After physical examination, children were sent to radiology department to take two views of x-rays for confirmation of flat foot, i.e., AP view &

lateral view. In AP view, the talo-navicular coverage angle was assessed.<sup>15</sup> Calcaneal inclination angle (CIA) & talo-calcaneal angle (TCA) were measured in lateral view of x-rays of foot.<sup>11,12</sup> For the radiological examination, a single parameter if found above the normal range, were considered as flat foot and were further labelled as rigid or flexible based on the clinical diagnosis (Figure 2 a-c).

The morphological structure of the foot was studied in standing position with the help of Podoscope. All the values were measured using podo-scanner (Podoscope-podoscanner 2D, Sensor Medica, Rome, Italy) which was imported from Italy, Rome. The patients were asked to stand bare footed on the Podoscope with 6 cm distance between both feet and arms were asked to keep at sides. Measurements of the planter side of foot were taken when load exertion on both feet was equal. Free Step software (Sensor Medica, Rome, Italy) saved and took the measurements of the foot prints. The software measured Clark's angle for longitudinal arches automatically. Arch index was measured by measuring foot length with the help of a calibrated scale on podoscopic footprint from end of 2nd metatarsal to hindfoot. This length was divided by 3 to demarcate foot into 3 parts as A, B and C. The arch index was calculated with the help of a formula  $AI = B/A+B+C$  (19, 23) (Figure 2 d-e).



**Figure-2:** a) Representative images of Talonavicular angle of  $10^\circ$  AP View. b) calcaneal inclination angle of  $17.4^\circ$ . c) talocalcaneal angle of  $54^\circ$ , d) podoscopic foot print measuring Clark's angle, e) I= Measurement of arch index in podoscopic foot print,  $AI = B/A+B+C$ , II= Flat footed patient having Clark's angle of 23 degrees

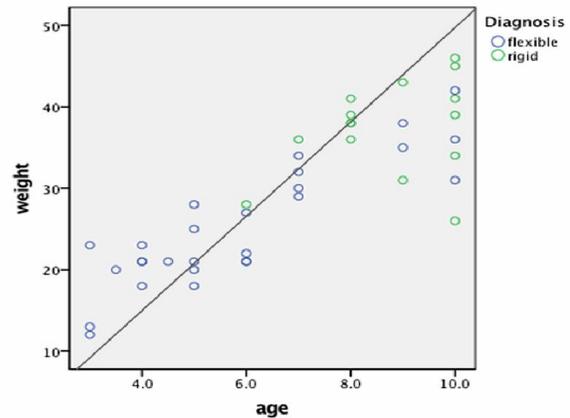
The analysis was done by using Statistical Package for Social Science (SPSS version 20.0) both qualitative and quantitative parameters. Independent t-test was performed to compare the parametric values for all the parameters for any significant difference between the two flat foot groups while Pearson's correlation coefficient was computed between different radiographic and podometric parameters; and demographic variables. Furthermore, sensitivity and specificity, positive and negative predictive values, positive and negative likelihood ratios of the measured parameters was also computed. ROC curve analysis was also carried out used to compare the diagnostic performance of different radiological and podometric parameters.<sup>18</sup> A 95% confidence interval and a  $p \leq 0.05$  was considered significant.

**RESULTS**

Demographically the data included age, gender, and weight of the patients. Of the two groups (flat footed and control group). The age range was from 3 to 10 years including pre-schoolers and school going children. The mean age of flat-footed children was  $6.88 \pm 2.68$  years and in control group, it was  $7 \pm 2.08$  years. The pre-schoolers were 14 in number and 28 children were school going in flat foot group while pre-schoolers in control group were 12 and school going children were 30 in number. In flat footed group, 25 children were males while 17 were females. While in control group, 23 children were males while female children were 19 in number. The weight of the patient was also recorded on weighing machine. The mean weight of the flatfooted group was  $30 \pm 8.94$  kg while in control group mean weight was  $27.8 \pm 8.24$  kg. The maximum weight recorded in flatfooted group was 48 kg and minimum weight was 12 kg while the maximum weight in control group was 45 and minimum weight in the same group was also 12 kg. A positive

association was observed between the age and weight of the patients when interpreted in terms of types of flat foot (Figure-3). The patients with flexible flat foot were younger and weigh less as compared with the patents with rigid flat foot.

Thus the incidence of rigid flat foot increased as the age and weight of the patents increased (Figure-3).



**Figure-3: A scatter plot showing a positive association between weight and age in relation with the flexible and rigid types of flat foot**

The main chief complaints of the patients with flat foot included pain in toes, calf pain, knee joint pain, difficulty in walking and pain in foot while standing from sitting position.

Out of 42 children with flat foot, 25 had positive family history of flat foot and 17 had no family history of flat foot. The summary of findings on clinical examination, radiology and podometry are summarized in table-1.

**Table-1: Summary of the findings on photography, radiology and Podometry**

Photography				
Parameters	Observations		Findings	
	Control	Flat foot group	Control	Flat foot group
GTE	Present/absent	Present in all	26.2% absent 73.80% Present	
Photography	Back view: Hind foot valgus	Absent	12 had hind foot valgus without fore foot abduction. 20 had both present.	
	Front view: Forefoot abduction	Absent	1 had fore foot abduction without hind foot valgus 9 had both absent	
FPI	Pronated foot	0	50%	
	Supinated foot	0	0	
	Neutral position	100%	50%	
Radiography				
	Control group		Flatfoot group	
	Mean±SD	Range	Mean±SD	Range
Talonavicular angle	5.65±1.43	3-7.2	6.50±0.57	3-20
Talocalcaneal angle	37.26±7.5	25-49	40.52±0.49	25.3-52.5
Calcaneal inclination angle	19.57±2.93	16-25.3	19.93±5.25	12-37
Podometry				
	Control group		Flatfoot group	
	Mean±SD	Range	Mean±SD	Range
Arch Index	0.32±0.005	0.32-033	0.32±17.58,	0.21-0.46
Clark's Angle	46.66±4.60	37-54	28.92±16.20	18-45

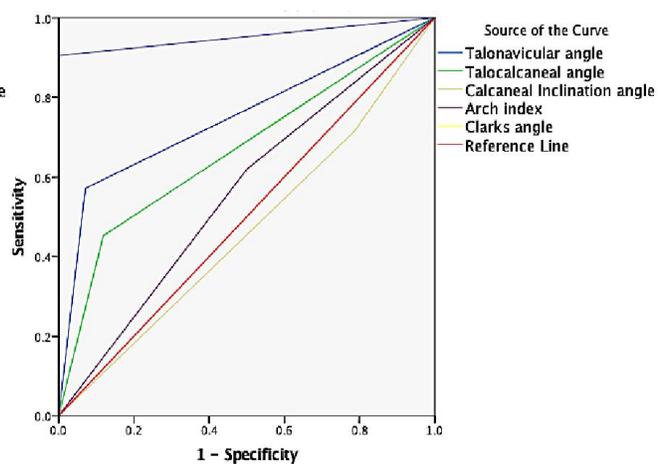
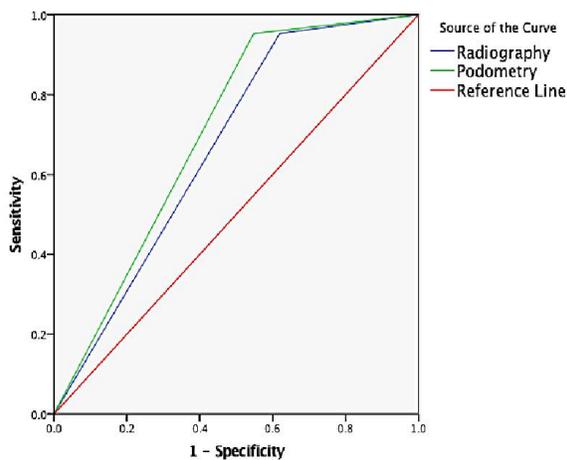
By keeping the clinical diagnosis as a gold standard, of 42 children in the flat foot group, 40 were found to be flat footed on radiological measurements and 36 on podometric measurements. Two children on x rays and 6 on podometry were normal in all measurements but were flat footed clinically. On the basis of individual parameters, a further breakdown of these children into flat foot and normal category is shown in table-2.

In order to compute sensitivity and specificity of the radiological and podometric parameters, the sample was divided into four different categories by keeping the clinical diagnosis as gold standard. The first category were true positives (those with flat foot on clinical diagnosis), true negatives (those with normal feet on clinical diagnosis), false positives (those who are normal on clinical diagnosis but labelled flat foot with either radiological or podometric parameters) and false negatives (those with flatfoot on clinical diagnosis but labelled normal on radiological or podometric parameters). Based on the above-mentioned categories, the data retrieved is mentioned in table 3. For sensitivity and specificity, the following formulas were used:

$$\text{Sensitivity} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Negative}}$$

$$\text{Specificity} = \frac{\text{True Negative}}{\text{False Positive} + \text{True Negative}}$$

In addition, positive and negative likelihood ratio as well as positive and negative predictive values were also computed and are mentioned in table-3. Comprehensively for radiological parameters, the sensitivity was computed to be 95.2%, while specificity was 69%. PPV was found to be 75.5% while NPV was 93.5%. Thus, the overall accuracy of radiological parameters was 82%. Similarly, for podometry, the sensitivity was 85.7% while specificity was 47.6% with PPV of 62% and NPV of 77%. Thus, the overall accuracy of podometry was 67%. Collectively radiographic parameters were found to be more sensitive in diagnosing flat foot than podometric parameters, however individually podometric parameters are more sensitive. Furthermore, Receiver Operating Curve analysis was carried out to determine how well each of these parameters as well as podometric and radiological parameters collectively can distinguish between the diseased and normal subjects (Figure-3). Between radiology and podometry, Area Under the Curve was more for podometry (AUC= 0.702) as against radiology (AUC=0.667). Among all diagnostic parameters, the area under the curve (AUC) was highest for Clark’s angle (AUC=0.952) and lowest for Calcaneal inclination angle (AUC=0.464). Among the radiological parameters, highest AUC was for Talonavicular angle (AUC=0.750).



**Table-2: Parametric details of flat foot sub types.**

	Parameters	Normal	Flatfoot						
			Total	Flexible			Rigid		
				n	Mean	Range	n	Mean	Range
X-ray	Talonavicular angle	15	27	14	8.45°	7-9.3°	13	7.93°	7-20°
	Talocalcaneal angle	21	21	10	47.22°	44-52.5°	11	48.16°	45-52.5°
	Calcaneal Inclination angle	12	30	22	17.14°	12-22.5°	8	17.75°	12-19.4°
Podometry	Arch Index	8	34	13	0.36	0.33-0.46	15	0.36	0.32-0.45
	Clark’s angle	4	38	20	28.85°	21-31°	15	25.86°	18-31°

**Table-3: Detailed breakdown of sensitivity, specificity of the radiological and podometric parameters**

Parameters	TP	TN	FP	FN	Sensitivity*	Specificity*	PPV	NPV	Accuracy
<b>Radiological parameters</b>									
Talonavicular angle	27	39	3	15	64% (48–78%)	92.86% (80.5–98.5%)	90%	72.2%	82%
Talocalcaneal angle	21	38	4	21	50% (34–97%)	90.4% (77–97.3%)	84%	64%	70%
Calcaneal Inclination angle	30	36	6	12	71% (55–84%)	85.7% (71–94.5%)	83%	75%	78.5%
<b>Podometric parameters</b>									
Arch Index	34	23	19	8	81% (65–91%)	54.7% (38.6–70%)	64%	74%	67.8%
Clark's angle	38	38	4	4	90% (77–97%)	90% (77–97%)	90.5%	90.5%	90.5%

TP=True positive, TN=True negative, FP=False Positive, FN=False Negative. \*Sensitivity and specificity with 95% CI. PPV=Positive predictive value, NPV=Negative predictive value

Independent t-test was also performed to compare the parametric values for all the parameters for any significant difference between the two flat foot groups i.e. rigid and flexible flat foot. The  $p$ -value was found to be insignificant for all comparisons except for Clark's angle where both the groups differed significantly ( $p=0.005$ ).

Correlation between different radiographic and podometric parameters was computed. A strong significantly positive correlation existed between arch index and talocalcaneal angle ( $r= .805, p=0.000$ ) while a significantly negative weak correlation existed between the 2 podometric parameters i.e. arch index and Clark's angle ( $r=-.367, p=0.017$ ). This suggests that increasing arch index will be associated with a decreasing Clark's angle and vice versa.

## DISCUSSION

Flatfoot is one of the major causes of clinical visits for patients with paediatric foot problems. Despite the high prevalence of paediatric flat foot, there is a lack of consensus on a classification and substantiated protocol for the management of the flat foot.<sup>21–23</sup> Although the diagnosis of flatfoot is usually based on clinical examination, its subjectivity has resulted in the emergence of a range of diagnostic tools such as visual inspection, anthropometry, imaging and podometry for the assessment of flat foot.<sup>24,25</sup> In this study, an attempt is made to determine the diagnostic accuracy of these available tools by keeping the clinical diagnosis as the gold standard. The results suggested that collectively radiological parameters are more specific while podometric are more sensitive in diagnosing flat foot. While individually, Clarks angle has the highest sensitivity among all the parameters studied. Furthermore, a combination of radiological and podometric parameters can lead to a more accurate diagnosis of paediatric flat foot.

It is a known fact that the flat feet prevalence correlates inversely with the age of the patient.<sup>22</sup> The age

group included in this study ranged from 3–10 years that comprised of pre-schoolers and school going children as the major development of foot arches occur in these years of a child's life.<sup>26</sup> Age is the main predictive feature in diagnosing flat foot as the risk of flat foot gradually decreases as age increases.<sup>13</sup> Also literature suggests that for appropriate management of flat foot, the age to start treatment is of utmost importance.<sup>22</sup> In our study, despite a small sample size, much variation res observed in terms of age at which these children presented with the complaint of flat foot. Furthermore, the history of the patients suggested that the parents paid relatively less attention to child's foot at an early stage of development and visited clinics until the deformity progressed and caused pain and disabilities resulting in either rigid or complicated flatfoot.<sup>27</sup> This observation was supported by the fact that in our study, the frequency of patients with rigid flat foot and increasing age was more than the flexible flatfoot. However, one explanation to this lack of reporting at an early stage is the anticipation of flatfoot getting resolved with age.

Apart from age, weight of the patient is also a concern as the chances of a preschool child being diagnosed as flat foot increases with increase in weight<sup>14</sup>, as with increasing weight, the medial longitudinal arch is depressed and flattened causing an increased contact of the foot with the ground.<sup>3</sup> In another study, plantar fat pad was analysed and compared to body weight of pre-schoolers.<sup>28</sup> Similarly, in our study, a positive association was observed between the age and weight of the patients in relation to the severity of the flat foot.

It has been suggested that boys are more predisposed to flat footedness than the girls owing to the differences in arch development.<sup>13,28</sup> Similar pattern was observed in our study. However, EI *et al.* in their study showed that females had greater tendency of flat footedness as compared to males due to increased mobility in joints.<sup>29,30</sup> These contradictory findings may be attributed not only to the contextual differences but

also to the differences in sample size and sampling techniques.

As far as the clinical examination is concerned, the great toe extension tests is considered gold standard in classifying patients into rigid and flexible flat foot.<sup>18,31</sup> Furthermore, for definite diagnosis of flat foot, a patient must have forefoot abduction, a collapsed medial longitudinal arch and hind foot valgus.<sup>32</sup> Foot Posture Index-6 is the widely used assessment tool that can visually measure the foot posture and determine the foot type of a patient.<sup>33,34</sup> Jung Su Lee *et al.* gave a positive correlation between FPI and paediatric radiographs and considered both of them as helpful clinical tools in diagnosis of flat foot.<sup>20</sup> Therefore, in our study, we combined FPI with great toe extension test and photography and considered it as gold standard for diagnosing and classifying patients with paediatric flat foot.

Two of the commonly used diagnostic tools in the management of flat foot issues are imaging and foot prints.<sup>15,18,22</sup> Usually, the patients with asymptomatic flat foot are not referred to radiology while for symptomatic flat foot, weight bearing radiographs are taken at different angles but findings are usually inconclusive.<sup>22,31</sup> On the other hand, it has been suggested that radiographs give mirror image of the bony composition of the medial longitudinal arch, hence can be regarded as definite assessment tool.<sup>17</sup> In our study we took the AP and lateral views radiographs of both the study groups in weight bearing position to determine the relation of talus with calcaneum.<sup>15</sup> Of multiple angles, which can be used to diagnose flat foot, we measured three most commonly used angles and assessed them for their reliability.<sup>23</sup> Also, the results of this study provided cut off values for radiographic assessment and classification of flat foot into flexible and rigid sub types. Other radiographic tools such as MRI or CT scans were not included in this study due to the lack of complicated flat foot. Also, these investigations are usually advised if there is a limited range of joint movement in the subtalar or midfoot region.<sup>22,35</sup> Furthermore, these investigations are done for surgical planning which was beyond the scope of this study.

Foot printing has long been considered as a reliable screening tool for flatfoot patients.<sup>14,15</sup> However, in this study, Podometric analysis of foot prints was carried out on a 2D podocan. We took the foot prints of the children by making them stand on the podocan bare-footed while the images were automatically saved in FREESTEP software (FREESTEP Standard version 2). Previously, rubber mats with non-greasy inks or plain ink pads were used for taking foot prints.<sup>24,36</sup> In this study we used modern method of foot printing which was not only non-invasive and easy to perform but also was quick, less troublesome for patients and

non-messy. The image taken was easily assessed and the patient was diagnosed on the spot. The only downside of this intervention was the cost. However, the extend of diagnostic accuracy achieved with this new intervention was very encouraging. The two podometric parameters measured in this study were arch index and Clark's angle, which were easily computable using FREESTEP software. Both arch index alone and Clark's angle along with Chippaux-Smirak index have previously been used for diagnosing flat foot in children.<sup>37,38</sup> In this study, the cut off values of both these parameters for flexible and rigid flat foot were also evaluated and compared with the normal ranges.

All the parameters were studied on a the right foot of all the patients since there is no significant difference between the anthropometric readings of both feet.<sup>32</sup> Among the radiographic parameters calcaneal inclination angle had the maximum sensitivity of 71% in diagnosing flexible and rigid flat foot, while among podometric parameters, Clark's angle was found to be 90% sensitive. These parameters have not been studied previously in terms of their sensitivity and specificity in diagnosing flat foot. Furthermore, in this study a strong significantly positive correlation existed between arch index and talocalcaneal angle while a significantly negative correlation existed between the 2 podometric parameters, i.e., arch index and Clark's angle. In a study by Chen *et al.*, failed to report any significant correlation between radiographic measurements and arch index.<sup>33</sup> In our study, a weak positive correlation existed between the talonavicular angle and weight of the patients as well as between the Clark's angle and patients' weight while no significant correlation was found between arch index and demographic variables of age and weight. Yalcin *et al.* correlated gender with arch index and found no major correlation between these two variables ( $r=-0.10, p \geq 0.05$ ).<sup>39</sup> H. Hazzaa *et al.* correlated age and flat foot and found no significance between them in both genders.<sup>40</sup> while in our study we noted that the incidence of flexible flat foot is higher among preschool children while rigid flat foot children were mostly from school going age group. However, Chen *et al.* reported that the incidence of flat foot decreased with increasing age because of its innate ability of auto correction as age advances.<sup>32</sup>

This study had its limitations. Due to short duration of the study, the sample size was relatively small. The cut off values as well as sensitivity and specificity of different diagnostic parameters may differ if larger sample size is taken. There was only one observer involved in the study so, the chances of biasness cannot be ruled out. Further research to develop more valid, reliable and clinically relevant foot posture measures, such as dynamic measures should be carried out. In addition, age specific cut off values for different paediatric age groups can be looked into. In

studies with single rater, interrater reliability should be carried out whilst validating these diagnostic parameters.

## CONCLUSION

This study demonstrated that the diagnostic accuracy of radiography was considerably more than the podometry. Among radiological measurements, calcaneal inclination angle was more sensitive than talonavicular and talocalcaneal angles while for podometry Clark's angle was found to be more sensitive than arch index. A strong positive correlation between arch index and talocalcaneal angle. Although children with flat foot are mostly diagnosed on clinical examination but the findings of our study are suggestive of combining radiological and podometric parameters with the findings on clinical examination, not only for the diagnosis but also for the accurate management of paediatric flat foot.

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## AUTHORS' CONTRIBUTION

All the authors have contributed profoundly to the concept, design and structure of the paper and are in agreement with the content of the manuscript, which has been penned keeping in mind the fundamentals of any standard publication.

NH: Collected the data and analysed. NB: Conceived, developed the idea, design, did manuscript writing and final approval. ZH, SJ: Reviewed and edited the manuscript. TR, AS: Helped in data collection and analysis.

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