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Research Article

ISOLATED ABSENT NASAL BONE IN PREDICTING CHROMOSOMAL ABNORMALITIES

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ABSTRACT

Objective: This study is aimed to evaluate the role of Isolated Absent nasal bone (IANB) in predicting chromosomal abnormalities, mainly Trisomy 21. The IANB cases are identified by ultrasound in first and second trimesters and then reviewed with karyotype obtained from amniotic fluid or chorionic villus sampling. Introduction: Identification of nasal bone forms the major part of imaging protocol in first and second trimester fetal imaging because, it has a significant association with abnormal fetal karyotype and considered as a major marker for aneuploidies, especially for Trisomy 21 and it is evident from many research articles of similarinterest. The ethnic difference in size of the nasal bone and the usefulness of itsevaluation in South Indian women, urged to perform this study. **Type of study**: Prospective study. **Sample population**: All pregnant women from January 2020 till June 2021 between 12 – 24 weeks gestational age who visited our genetic clinic were screened for Nasal bone and cases with IANB only were included in the study. Karyotype of 100 IANB cases were evaluated for chromosomal abnormality. Methods: All pregnant women presenting to the Genetic Clinic from January 2020 through June 2021 with ultrasound finding of absent or hypoplastic nasal bone either in the first or second trimester were prospectively enrolled in the study, after obtaining informed consent. Patients who had IANB or hypoplastic nasal bone were included in the study and those with associated anomalies were not included. **Results** : We studied 283 women who were identified with absent nasal bone. Total of 102 patients underwent invasive testing, of which 1 CVS sample had inadequate sample and 1 amniocentesis resulted in culture failure. The amnioticfluid was sent for QFPCR and karyotyping. Out of 100 only 9 fetuses (9%) had TRISOMY 21 and out of which 1 was Mosaic variant. **Conclusion:** Our study shows that IANB was associated with Trisomy 21 in 9 % of cases which concurred with other literatures of similar interest. We recommend that if IANB is associated with other anomalies, the fetuses should always be assessed for chromosomal abnormalities by invasive testing as the risk varies between 30 – 40 %. In isolated cases, patient should be counselled and reassured, but termination of pregnancy should not be encouraged without karyotyping. Also we suggest to perform both Karyotyping and QFPCR to detect more cases of mosaicism than either alone.

Keywords :- Isolated Absent nasal bone, Chromosomal Abnormalities, South Indian women.

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INTRODUCTION

Ultrasound is the primary modality for prenatal evaluation for structural abnormalities and to identify markers in detecting aneuploidies. Identification of nasal bone forms the major part of imaging protocol in first and second trimesterfetal imaging because, absent nasal bone has a high association with abnormal fetal karyotype and it is considered as a major marker for aneuploidies, especially for Trisomy 21. Soft markers are indirect ultrasound findings which has rare or no pathological

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significance and are frequently identified in aneuploidy fetuses. Soft markers are classified as major and minor of which majority of them have adverse pregnancy

outcomes including intrauterine fetal demise, preterm deliveries, restricted fetal growth and infections.

The main objective of this article is to evaluate the diagnostic importance of absent nasal bone and its association with abnormal karyotype. In our population, the incidence of chromosomal abnormalities occur in less than 0.5%of live births out of which Down's syndrome is the most significant one. In our sample population, absent nasal bone goes mostly undetected in first trimester evaluation, the main reasons are – majority of the screening is done by non- FMF certified NT specialists who are unaware of the significance of detecting an aneuploidy marker and the patients themselves miss the first trimester screening due to lack of awareness. So this topic throws more light on how vital is detection of absent nasal bone and its association with chromosomal abnormality.

The nasal bone develops through an intramembranous ossification process and are usually not demonstrable histologically in fetuses with crown-rump length less than 42 mm. Nasal hypoplasia is one of the features described by Langdon Down in 1866 in his manuscript "Observations on an ethnic classification of idiots " and associated to a delayed ossification process that sonographically corresponds to an absent NB in first trimester and to an absent or hypoplastic NB in the second-trimester anomaly scan. Absent nasal bone is found in about 65% of Down's fetuses and 1%–3% of the normal fetuses during the first trimester [20].

Absent nasal bone is not considered as a fetal malformation per se however it is a marker of fetal aneuploidy, specific for common trisomies. The nasal bones are actually paired structures, there is a right and a left nasal bone, and there can be unilateral as well as bilateral absence or hypoplasia. Absent nasal bone is seen in 60 % of fetuses with trisomy 21, 53 % of trisomy 18 and in 45 % of trisomy 13; its absence confers a likelihood ratio of 27.8 for Down syndrome; furthermore, it can be seen in 2.5 % of euploid fetuses [19]. Among euploid pregnancies absent nasal bone is seen more frequently in African American women (5.8 %) than in white women (2.6 %) or Asian women (2.1 %) [20]. In a recent publication among 57 fetuses with absent nasal bone and normal karyotype three fetuses had an adverse outcome and, in all, additional sonographic abnormalities were seen[20].

Ultrasound and biochemical markers

The association in the first trimester fetus of increased nuchal fluid and aneuploidy was first described more than two decades ago, and this finding hasled to the establishment of first trimester aneuploidy screening with NT and biochemical markers. A thickened NT has been correlated with the presence of trisomy 21 and fetuses have a mean NT thickness of 3.4 mm. In a study involving 654 fetuses with T21, more than half were shown to have an NT ≥3.5 mm. The NT in the normal fetus increases with increasing crown-rump length (CRL) measurement and NT screening has been successfully used to adjust the pregnancy's aneuploidy a priori risk established by maternal age. This has been one of the most important elements of aneuploidy screening as it resulted in a significant reduction in unnecessary invasive testing on pregnant women with advanced maternal age. In pregnancies with T21 fetuses, the maternal serum concentration of free β-human chorionic gonadotropin (β-hCG) is about twice as high and pregnancy-associated plasma protein A (PAPP-A) is reduced to half compared to euploid pregnancies.NT measurement alone identifies about 75% to 80% of T21 fetuses, the combination of NT with maternal biomarkers in the first trimester increases the T21 detection rate to 85% to 95%, while keeping the false-positive rate at 5%. Indeed, in a recent prospective validation study of screening for trisomies 21, 18and 13 by a combination of maternal age, fetal NT, fetal heart rate and serum free β-hCG and PAPP-A at 11+0 to 13+6 weeks of gestation in 108,982 singleton pregnancies, T21, 18, and 13 were detected in 90%, 97%, and 92% respectively with a false-positive rate of 4%. Monosomy X was also detected in more than 90% of cases along with more than 85% of triploidies and more than 30% of other chromosomal abnormalities. In addition to NT, other sensitive first trimester ultrasound markers of T21 include absence or hypoplasia of the nasal bone, cardiac malformations with or without generalized edema , tricuspid regurgitation , aberrant right subclavian artery and increased impedance to flow in the ductus venosus .

Assessment of the Nasal Bone

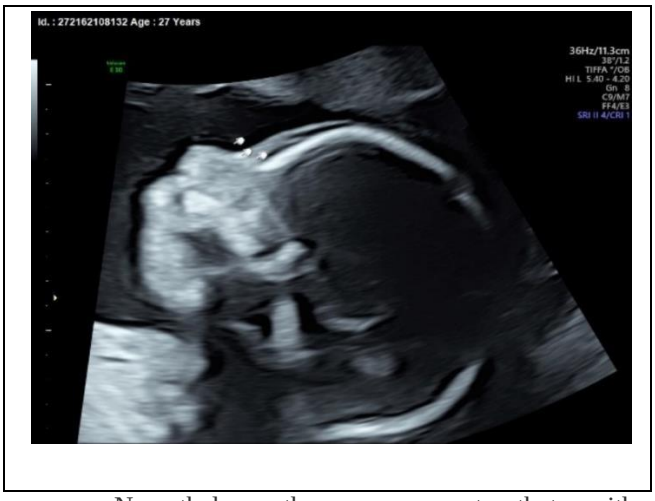
Technique :

Once the midsagittal plane has been obtained, it would be necessary to tilt gently the probe from one side to the other of the fetal face to ensure an adequate examination of the NB. The NB can be identified in a midsagittal or, when a gap between the NBs of 0.6 mm or more is present (9%of fetuses), in a slightly parasagittal plane [21].

Evaluation for presence or absence of the nasal bone can be performed during the first trimester imaging. Nasal bone ossification first becomes apparent at a crown rump length of approximately 42 mm or 11 weeks gestation and nasal bone length progressively increases with gestation. But in our study to avoid false positives and considering the rural population, we confirmed absent nasalbone only after 12 weeks of gestation. Assessment for presence of the nasal bone is performed according to FMF guidelines – image taken the midsagittal plane and,

as for NT measurement, requires strict adherence to proper technique and operator experience to be reliable.The nasal bone appears as an echogenic line parallel to and thicker than the echogenic skin line overlying the nasal bridge(Fig.2). It is best seen when the footplate of the transducer is parallel to the long axis of the nasal bone. The two parallel lines of the nasal bone and skin line comprise the "equal sign". The nasal bone is considered absent if the deeper line is not present (Fig.1). Nasal bone assessment appears to be more difficult than NT assessment.

Figure 1 : Absent nasal bone in second trimester



Nevertheless, there are reports that, with adequate training and experience, assessment for presence or absence of nasal bone can be performed with success in up to 99 % of fetuses [2]. In order to define this marker as "present," the NB must be brighter and thicker than the skin above it. It may beuseful to note that the NB is visible on the scan, following the above-described technique, usually as a single line, even if the bones are actually two [5]. The ultrasound signal of brightness due to the calcium present in the bones, simply overlaps, and therefore, the bones show up as a single bright line. As aforementioned, when the gap is greater than 0,6 mm, the NB may not be clearly visualized in a perfectly midsagittal view; in these circumstances, which account for 9% of the cases, the transducer should be carefully tilted to a parasagittal plane on either side of the midline to visualize the two NBs. The incidence of absent NB, as previously mentioned, is 1%–3% in normal fetuses, and it could depend on gestational age (more frequent around 11 weeks of gestation than later), ethnicity, and constitutional factors [20].

Significance of Absent Nasal Bone

As mentioned, an absent nasal bone is seen more frequently in trisomy 21 as compared to the general population. In a study of over 21,000 fetuses between 11 and 14 weeks, absence of the nasal bone was noted in 62 % of fetuses with trisomy 21 as compared to 0.6 % of unaffected fetuses [2]. Absence of nasal bone has been shown to be an independent finding with respect to serum β- hCG and PAPP-A and can, therefore, be added to routine combined prenatal screening for trisomy 21 [1]. When combined with routine NT screening and serum β-hCG and PAPP-A, addition of nasal bone presence may decrease the false positive rate for trisomy 21 from 5 to 2.5 % [1]. Absence of the nasal bone has also been reported in approximately 55 % of fetuses with trisomy 18, 35 % of trisomy 13, and 10 % of Turner's syndrome [3].

It is important to be aware that an absent or hypoplastic nasal bone does not necessarily imply pathology and can be a normal variant. The prevalence of absent nasal bone decreases with gestational age and absence of the nasal bone prior to a crown rump length of 42 mm should not be considered abnormal. If there is question of nasal bone absence between 11 and 12 weeks, a repeat scan can be obtained to ensure that lack of visualization represents true absence, as opposed to late ossification. Additionally, there is ethnic variation in presence and size of the nasal bone and an absent nasal bone may be more prevalent in certain ethnic groups, particularly African and Asian populations. A prospective study of nearly 4000 fetuses reported prevalence of absent nasal bone to be 5.8 % in patients of African origin, 3.4 % in patients of Asian origin, and 2.6 % in patients of Caucasian origin [4]. In some instances, the nasal bone may be present but seen to be shortened or hypoplastic. Nasal bone length has not been shown to be a useful first-trimester measurement for screening of trisomy 21 [1].

In addition to nuchal translucency, evaluation of the fetal nasal bone is a benefit of first trimester ultrasound. Hypoplastic or absent nasal bone has been associated with fetal Down syndrome. Nasal bone evaluation between is included in first-trimester screening for Down syndrome as it is independent of other first-trimester markers (free βhCG, PAPP-A, and NT). In one series, the nasal bone was absent in 2.6 % of the euploid fetuses (though this may vary with ethnicity); it was absent in 59.8 % of the fetuses with trisomy 21, 52.8 % with trisomy 18, 45.0 % with trisomy 13 and in none of the fetuses with Turner syndrome [18]. At a false-positive rate of 5 %, nasal bone evaluation in addition to NT and serum analytes was estimated to achieve a sensitivity of >95% for trisomy 21, 18 and 13, and is not thought to significantly prolong ultrasound examination time [18,19].

The absence of the nasal bone (NB) is considered a soft marker for aneuploidy.A soft marker is

a sonographic finding that can be associated with, but is not diagnostic of a fetal condition [10]. In the midsagittal plane, the NB is seen as a bright line of greater echogenicity than the skin. The presence of the NB is best assessed at a CRL between 65 and 84 mm correlating to a gestational ageof 13–13 + 5 weeks[11]. Criteria for measurement of the nasal bone can be seen in Table 1.

Figure 2: Nasal bone evaluation in First Trimester

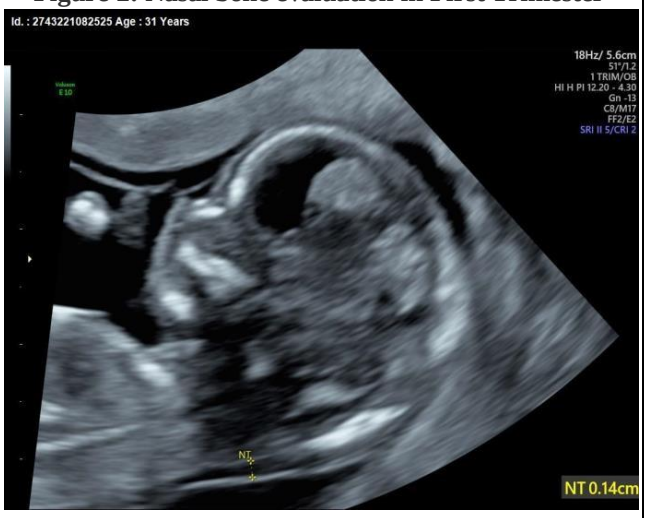


Table 1: Criteria to measure Nasal bone in first trimester – FMF guidelines

Fetal head, neck and thorax should occupy the entire image
Measured in the midsagittal view
Echogenic tip of nose should be seen
Third and fourth ventricle seen
Rectangular palate should be seen
Angle of insonation ~45° to fetal profile
Brightness of NB equal to or greater than

A hypoplastic or absent NB has been associated with trisomy 21. One publication reviewed over 35,000 NB examinations from nine different studies and showed that the NB was absent in 65 % of fetuses with trisomy 21 but only in 0.8 % of chromosomally normal fetuses [12]. In the second trimester, this marker becomes less predictive with absent NB seen in 30–40 % of fetuses with trisomy 21 and 0.3–0.7 % of chromosomally normal fetuses [13]. Differentmethods of reporting observations of the NB yield different results. Some report the NB categorically as “present” or “absent,” while others measure it and reportwhether it is hypoplastic. Absent NB in the second trimester was seen in 30–40% of fetuses with trisomy 21 and 0.3–0.7 % of chromosomally normal fetuses. By considering NB hypoplasia or absent nasal bone as a single category, the finding was seen in 50–60 % of fetuses with trisomy 21 and 6–7 % of chromosomally normal fetuses [13]. Other ways to report hypoplasia of the NBinclude an absolute cutoff of <2.5 mm, gestational age-related cutoff of <2.5th or <5th percentile, a ratio of BPD/NB length or multiples of the median for gestational age with <0.75 MoM being the cutoff for abnormal NB measurement [14 , 15]. It is noteworthy that there is natural variation in the appearance of theNB. Absence of the NB at or before 13 weeks gestation can be a result of delayed ossification instead of absence or hypoplasia [16]. Similarly, ethnic variations exist in the presence and size of the nasal bone. In a study by Cicero et al. the likelihood ratio for trisomy 21 with an absent NB was higher in Caucasian women than in Afro-Caribbean women (likelihood ration of 31 vs. 9) [17]. These variations reinforce that assessment of the NB should not be used in isolation for diagnosis of trisomy 21. On the contrary, it has been used in combination with first-trimester serum screening and NT measurement to increase the detection of trisomy 21–90 % over the 85 % of first trimester combined screening alone [18]. Evaluation of values of nasal bone length by comparing with both the Western and Indian data revealed that in 8 cases, the nasal bone length was small by Western standards, however by Indian charts the value was normal for the gestational age (more than 5 centile). The amniotic fluid culture analysis showed normal karyotype in all the 8 cases.

We wanted our study to be different from the earlier literature which dealt with absent Nasal bone. Firstly, we focused on cases only with IANB and omitted cases with associated anomalies. Secondly, wanted to know the exact association of IANB with Chromosomal abnormalities, which will help the fetal medicine consultant to counsel and reassure the patient when the fetus has IANB . Thirdly, we performed the study only after 12 weeks to avoid false positives and included patients until 24 weeks gestation, just to know how many patients are getting undetected in late second trimester. Fourthly , for all first trimester cases we did a combined transabdominal and transcervical approach which helped in identifying cases with patients having high BMI and technically difficult cases , otherwise those would have gone undetected or identified in second trimester only. Lastly, we wanted this study to create awareness among the local population on importance first trimester screening and significance of identifying nasal bone as early as possible and manage them accordingly.

Objective - To evaluate the percentage of chromosomal abnormalities infetuses with isolated Absent nasal bone.
Type of study: Prospective

Sample – All pregnant women who visited our genetic

clinic between 12 – 24 weeks of gestation were screened for nasal bone in accordance with strict FMF guidelines and those fetuses with IANB who were willing for invasive testing alone were included in our study. Once we reached 100 women who underwent invasive testing we completed the study.

Inclusion criteria :

i) Pregnant women between 12- 24 weeks of gestation with isolatedabsent nasal bone and willing for invasives.

Exclusion criteria :

i). Absent nasal bone with associated anomalies

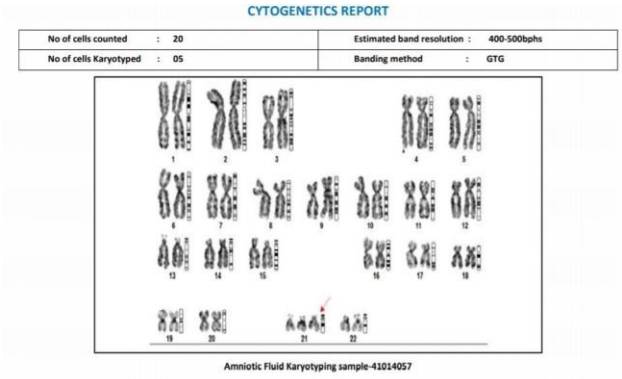
ii). Patients who were not willing for invasive testing

iii0. Patients who were tested positive in NIPT

Methods

All pregnant women presenting to the Genetic Clinic from January 2020 through June 2021 with ultrasound finding of absent or hypoplastic nasal bone in either first or second trimester of pregnancy were prospectively enrolled in the study, after obtaining informed consent. Nasal bone assessment was performed on allpregnant women between 12 – 24 weeks gestation by FMF Certified NT specialist in South Indian1. population for a period of 18 months. The criteria to consider nasal bone hypoplasia was nasal bone length less than 2.5th percentile for the period of gestation as described by Cicero et al. [3]. The values of hypoplastic nasal bone length concurred with the available Indian standards [11]. The ultrasound images of the nasal bone were analyzed to confirm that nasal bone was measured correctly. The presence of other associated soft markers for aneuploidies, along with results of biochemical screening was also recorded. The biochemical screening included the first trimester, triple or quadruple tests. All the patients with an isolated hypoplastic nasal bone were counseled for the appropriate invasive testing which included chorionic villus sampling or amniocentesis. The referrals were from multiple centres but Chorionic villous biopsy and amniocentesis were carried out in a single ultrasound unit and samples were sent to labs with College of American Pathologists (CAP) accreditation (Figure 3). The results were evaluated after performing invasive testing and evaluating the karyotyping for 100 cases of IANB. FMF prescribed guidelines were used for nasal bone assessment and the approach was combined transabdominal and transcervical in first trimester, transabdominal approach in second trimester. In absent nasal bone cases, which were identified in the first trimester and in patients who were not willing for Biochemical markers, the risk was assessed by using FMF software. In patients who missed their first trimester screening, the risk was calculated by Likelihood ratios and taking age risk as apriori risk. The cases were omitted for our study even if any other additional marker was identified in genetic sonogram. If the risk was high (1: 250) invasives were offered as the first choice and if the risk was intermediate (1:250 – 1: 1000) NIPS or invasive testing was offered . The study was carried out until karyotype was obtained for 100 fetuses with IANB.

Figure 3 : Karyotype report of Trisomy 21 with Isolated Absent nasal bone



Results

We screened 7823 pregnant women over a period of 18 months from January 2020 till June 2021 for absent nasal bone, in which 283 (3.6%) women were identified with absent nasal bone (Table 4). 152 cases (1.9%) had associated anomalies in addition to absent nasal bone, hence they were not included in this study and 131 cases with IANB (1.7%) . 72 cases were identified in first trimester and 190 cases were identified between 19- 22 weeks and 21 cases were identified between 22 to 24 weeks gestation. 30 patients underwent NIPS as they were not convinced to undergo invasive testing . NIPS was done in 19 patients during first trimester and 11 in between 16-18 weeks. Out of which 5 cases turned out to be screen positive, 1 patient terminated without invasive testing and remaining 4 were confirmed in karyotype also. The patients who underwent invasive testing were explained about the significance of absent nasal bone and its association with chromosomal abnormality. The risk and benefits of invasive testing, national and local percentage of post procedural fetal loss and maternal complications were thoroughly explained.

Amniocentesis was done in patients after getting informed consent. 28 patients in first trimester were willing for Chorionic villous sampling and 23 patients werewilling for amniocentesis between 16 – 19 weeks , 32 patients in between 19 –22 weeks and 19 patients in between 22- 24 weeks underwent amniocentesis. Total of 102 patients underwent invasive testing, of which 1 CVS sample had inadequate sample and 1 amniocentesis resulted in culture failure.

The samples were sent for Quantitative fluorescent polymerase chain reaction (QFPCR) and Karyotyping. Out of 100 only 9 fetuses (9%) had TRISOMY 21 and out of which 1 was Mosaic variant. (Table 5)

Our results stated that 9 % of the fetuses with absent nasal bone had chromosomal abnormalities which concurs with various literatures relevant to the same topic. However, the risk involved is much higher when it is associated with additional structural anomalies and abnormal biochemical values in first trimester double markers and quadruple screening in second trimester. It is also evident from our study, that all the cases with chromosomal abnormalities had only Trisomy 21 (100%).

Table 2: Distribution of study participants according to time of diagnosisof absent nasal bone (n=283)

Participants with absent nasal bone	Frequency	Percent
Diagnosed in First trimester	72	25.4
Diagnosed between 19-22 weeks	190	67.2
Diagnosed between 22 - 24 weeks	21	7.4
Total	283	100

Pie chart showing distribution of study participants according totime of diagnosis of absent nasal bone (n=283)

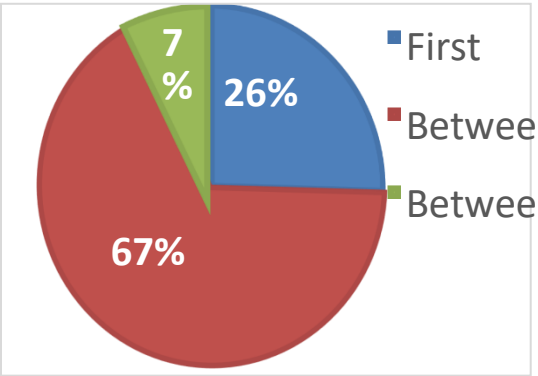


Table 3: Evaluation of Absent nasal bone for Trisomy 21 (n=7823)

Absent nasal bone	Trisomy 21	Euploidy	Total
Present	9	274	283
Absent	*0**	*7540**	7540
Total	9	7814	7823

* We calculated the following Parameters assuming that all cases without Absent nasal bone to be euploid (Though it is a strong assumption, it was not feasible & ethical option to perform karyotyping in all screened participants)

Statistics for Absent nasal bone	**Value**	**95% CI**
Sensitivity*	100.00%	66.37% to 100.00%
Specificity*	96.49%	96.06% to 96.89%
Positive Likelihood Ratio*	28.52	25.39 to 32.04
Negative Likelihood Ratio	0.00	-
Disease prevalence	0.12%	0.05% to 0.22%
Positive Predictive Value	3.18%	2.84% to 3.56%
Negative Predictive Value	100.00%	-
Accuracy	96.50%	96.07% to 96.89%

The only parameter that can be calculated without this assumption was Positive predictive value (PPV) which was 3.18% with 95% CI ranging between 2.84% to 3.56%.

Therefore, the post-test probability of having Trisomy 21 after a woman being diagnosed with absent nasal bone was roughly 3%. Furthermore, it has to be noted that the post-test probability as indicated by Positive predictive value (PPV) is not a constant and will vary according to the prevalence of Trisomy 21with PPV rising with rising prevalence and vice versa. Therefore, the pre-test probability of the disease (given by the prevalence of Trisomy 21) along with PPV of roughly 3% determines the post-test probability of having Trisomy 21.

Table 4: Overall prevalence in local population

Total pregnant women screened	7823
Total cases with absent nasal bone	283 (3.6 %)
Absent nasal bone with associated anomalies	152 (1.9%)
Isolated absent nasal bone	131 (1.7%)
Number of Invasive procedures	102
Sample failures / culture failure	2
No of Karyotype reports	100
Confirmed cases with Chromosomal abnormalities	9 (0.1%)
Confirmed cases of Trisomy 21	9 (0.1%)

Table 5 : Incidence of chromosomal abnormality in IANB cases

Total Absent nasal bone cases	283
ANB with other anomalies	152 (53.7%)
IANB	131 (46.3%)
Number of patients willing for invasive testing	102 (36.1 %)
Number of chromosomally abnormal fetuses	9 (3%)
Number of cases with Trisomy 21	9(3%)

Discussion

Detection of chromosomal abnormalities from ultrasound markers is a challenging task for the sonologists. Early detection, appropriate counseling and skilled invasive testing forms the essential trio in detecting Trisomy 21 in fetuses with absent nasal bone. Apart from our study, we did amniocentesis for fetuses with absent nasal bone and associated anomalies, in which the percentage of chromosomal abnormalities were much higher than in isolated cases. Hence , we conclude that if we identify absent nasal bone in first and second trimester ultrasound , atleast 9 % of fetuses will have associated chromosomal abnormality , mainly Trisomy 21 and the percentage increases significantly if there are multiple structural anomalies / markers identified in first and second trimester screening .

Conclusion

In our study based on south Indian population, we have concluded that 9 % of fetuses with isolated absent nasal bone will have chromosomal abnormality, especially Down's syndrome . Hence, the detection rate of Down's syndrome can be improved by appropriate identification of nasal bone either in first or second trimester. The identification of nasal none should be incorporated in imaging protocol and care should be taken that images should be acquired with strict FMF guidelines to avoid false positives. The early detection of Down's syndrome and other chromosomal abnormalities enables the patient to give a choice of continuing the pregnancy or terminating and also significantly helps in reducing the psychological and emotional stress if identified as early as possible. The use of Isolated Absent NB in the second trimester US may not be an effective screening tool for Down's syndrome. When absent nasal bone was associated with ultrasound anomalies, or with high risk in biochemical studies, there is a significant increase of abnormal chromosomes (41 % and 29 % respectively). So is recommended that if ANB is associated with other anomalies, the fetuses should always be assessed for chromosomal abnormalities by invasive testing. Furthermore, if Indian standards derived for nasal bone length are used, the yield is much higher as there are ethnic variations in measurement of the nasal bone. We recommend to perform both Karyotyping and QFPCR to detect more cases of mosaicism rather than either alone.

Presence of second trimester soft markers or any structural abnormality shouldbe carefully searched for by a fetal medicine specialist when absent NB is detected in second trimester. The cases of Isolated absent nasal bone should be reassured strongly for an expected positive outcome of the baby , however the patients should be counselled and informed there is roughly about 10 % chances that the fetuses can be affected with Trisomy 21 which can be confirmed only by invasive testing and termination of pregnancy should not be encouraged before undergoing fetal karyotype.

REFERENCES

1. Sonek JD, Cicero S, Neiger R, Nicholaides KH. Nasal bone assessment in prenatal screening for trisomy 21. Am J Obstet Gynecol. 2006;195:1219–30.
2. Cicero S, Avgidou K, Rembouskos G, Kafan KO,Nicolaides KH. Nasal bonein fi rst-trimester screening for trisomy 21. Am J Obstet Gynecol.2006;195(1):109–14.
3. Cicero S, Rembouskos G, Vandercruys H, Hogg M,Nicolaides KH. Likelihood ratio for Trisomy 21 in fetuses with absent nasal bone at 11–14 week scan.Ultrasound Obstet Gynecol. 2004;23:218–23
4. Prefumo F, Sairam S, Bhide A, Penna L, Hollis B, Thilaganathan B. Maternalethnic origin and fetal nasal bones at 11–14 weeks of gestation. BJOG.2004;111:109–12.
5. Odibo AO, Sehdev HM, Dunn L, et al. The association between fetal nasal bone hypoplasia and aneuploidy. Obstet Gynecol. 2004;104:1229–33.
6. Absent nasal bone, Society for Maternal-Fetal Medicine; Beryl R. Benacerraf, MD; Bryann Bromley, MD; Angie C. Jelin, MD
7. Dukhovny S, Wilkins-Haug L, Shipp TD, Benson CB, Kaimal AJ, Reiss R. Absent fetal nasal bone: what does it mean for the euploid fetus? J UltrasoundMed 2013;32:2131–4
8. Moreno-Cid M, Rubio-Lorente A, Rodriguez MJ, et al. Systematic review andmeta-analysis of performance of second-

trimester nasal bone assessment in detection of fetuses with Down syndrome. Ultrasound Obstet Gynecol 2014;43:247–53.
9. Morris JK, Wald NJ, Watt HC. Fetal loss in Down syndrome pregnancies.Prenat Diagn. 1999;19(2):142–5.
10. Ville Y. What is the role of fetal nasal bone examination in the assessment of risk for trisomy 21 in clinical practice? Am J Obstet Gynecol. 2006;195(1):1-3.
11. Rosen T, D'Alton ME, Platt LD, Wapner R, Nuchal Translucency Oversight Committee MFMF. First- trimester ultrasound assessment of the nasal bone to screen for aneuploidy. Obstet Gynecol. 2007;110 (2 Pt 1):399–404.
12. Moreno-Cid M, Rubio-Lorente A, Rodriguez MJ,Bueno-Pacheco G, Tenias JM, Roman-Ortiz C, et al. Systematic review and meta-analysis of performanceof second-trimester nasal bone assessment in detection of fetuses with Down syndrome. Ultrasound Obstet Gynecol. 2014;43(3):247–53.
13. Cicero S, Sonek JD, McKenna DS, Croom CS,Johnson L, Nicolaides KH.Nasal bone hypoplasia in trisomy 21 at 15–22 weeks' gestation. Ultrasound Obstet Gynecol. 2003;21(1):15–8.
14. Odibo AO, Sehdev HM, Stamilio DM, Cahill A, Dunn L, Macones GA. Defining nasal bone hypoplasia in second-trimester Down syndrome screening:does the use of multiples of the median improve screening efficacy? Am J Obstet Gynecol. 2007;197(4):361.
15. Benacerraf B. Sonographic findings associated with fetal aneuploidy.Waltham, MA: UpToDate; 2014
16. Cicero S, Rembouskos G, Vandecruys H, Hogg M,Nicolaides KH. Likelihood ratio for trisomy 21 in fetuses with absent nasal bone at the 11–14-week scan.Ultrasound Obstet Gynecol. 2004;23(3):218–23.
17. Cicero S, Avgidou K, Rembouskos G, Kagan KO,Nicolaides KH. Nasal bonein first-trimester screening for trisomy 21. Am J Obstet Gynecol. 2006;195(1):109–14.
18. Haak MC, Twisk JW, Bartelings MM, Gittenberger-de Groot AC, van Vugt JM. First-trimester fetuses with increased nuchal translucency do not show altered intracardiac flow velocities. Ultrasound Obstet Gynecol. 2005;25(3):246–52.
19. Malone FD, Ball RH, Nyberg DA, Comstock CH, Saade GR, Berkowitz RL, et al. First-trimester septated cystic hygroma: prevalence, natural history, and pediatric outcome. Obstet Gynecol. 2005;106(2):288–94.
20. Peralta CF, Falcon O, Wegrzyn P, Faro C, Nicolaides KH.Assessment of the gap between the fetal nasal bones at 11 to 13 + 6 weeks of gestation by three-dimensional ultrasound. Ultrasound Obstet Gynecol 2005; 25(5): 464–7.

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