CHAPTER 1

INTRODUCTION

1.1 IDENTIFICATION OF PROBLEM

Medical Imaging is an essential tool for improving the diagnosis, understanding and treatment of a large variety of diseases. Down Syndrome (DS) has been found to be the most common chromosomal Aneuploidy which results in abnormal live birth. This has been first described by John Langdon Down, the British physician in 1866. Recently as per the reports of the World Health Organization (WHO) nearly 35% of DS population has been noticed in India. This has facilitated the research to diagnose DS at the early stage by extracting the features of fetus. Many techniques using invasive and non-invasive approaches have been proposed to identify the DS for better diagnosis. It has also been reported that the non-invasive techniques outperform the invasive techniques due to the drawbacks in the latter may cause loss of pregnancies.

In the past century, the technologies have advanced due to the discovery of X-rays, Arteriography, Magnetic Resonance Imaging (MRI), Magnetic Resonance Angiography (MRA), Computed Tomography (CT), Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT) and Ultrasonography. These technologies have helped the physicians in making diagnostic decision with high accuracy.
The advancements in the field of computer and computing techniques have enhanced the diagnosis techniques to develop Medical Decision Support System (MDSS) to assist the medical practitioners for objective diagnosis and clinical pathology. Ultrasound plays a major role in diagnostic testing for Down syndrome also called as Trisomy 21. Prenatal sonography has been found effective for diagnosing the affected fetus based on the sonographic features using soft computing techniques.

With the advent of medical imaging modalities that provide different measures of internal anatomical structure and function, physicians are now able to perform typical clinical tasks such as patient diagnosis and monitoring effectively. Ultrasound (US) imaging finds wide applications in the diagnosis of human vascular system due to its real time, non-invasive, non-radioactive and inexpensive nature (Jegelevicius and Lukosevicius 2002, Pierre-Jean Touboul 2002). Besides the qualitative information for visual interpretation the quantitative information on the ultrasound scans, such as the sizes, edges and positions of anatomical structures, are also of significant interest for computer aided diagnosis. However the automatic analysis of ultrasound images is a difficult task because of the appearance of speckle patterns caused by the de-phased echoes from the scatterers. Analysis of ultrasound images is complex due to the presence of speckle noise (Loizou 2002, Sheng 2004).

The speckle often obscures and masks diagnostically important features in US images and hence speckle reduction is a critical preprocessing step for feature extraction, analysis and recognition from medical US imagery measurements (Czerwinski 1998, Jun Xie 2006). This has initiated the researchers to develop better medical diagnosis modules and reliable decision support system. Medical Decision Support System (MDSS) is being
concentrated to use image processing concepts and neural network techniques to assist the physicians in making objective decisions during diagnosis.

The solution to develop such a MDS system for identifying the normal and abnormal subjects is in high demand and to be addressed. In view of the above identified problem in fetal structure, systematic investigations including image processing and feature extraction have been proposed in the present investigation.

1.2 REVIEW OF LITERATURE

Down syndrome, Down's syndrome, or Trisomy 21 is a chromosomal disorder caused by an error in cell division that results in the presence of an additional third chromosome in chromosome 21 (Lejeune et al 1959). Down syndrome is the most frequent genetic disorder causing mild to moderate mental retardation and associated medical problems. It occurs in all races and economic groups. Down syndrome is associated with some impairment of cognitive ability and physical growth as well as facial appearance (Lejeune 1959). Individuals with Down syndrome tend to have a lower than average cognitive ability, often ranging from mild to moderate developmental disabilities. A small number have severe to profound mental disability. The incidence of Down syndrome is estimated at 1 per 800 to 1,000 births (Nicolaides 1992, Nicolaides 2004).

The existing diagnostic tests for down syndrome, though reliable, cause fetal miscarriages and result in medical complications for both the child and the mother. Hence it has been felt that there is a need to develop a less complex, affordable, non-invasive test procedure with minimal false detections.
Literature studies reveal that non invasive, US fetal image analysis have been used to identify the soft markers in the detection of Down syndrome. There are several markers for the detection of Down syndrome from US images of which Nuchal Translucency measurement is one. It is a useful marker for identification of patients at high risk of DS. There is a well established association between increased first trimester Nuchal translucency thickness and chromosomal abnormality.

Nicolaides et al (1992) described an association with fetal Nuchal Translucency and prediction of abnormal fetal karyotype in the First trimester screening study. The study concluded that fetal Nuchal Translucency thickness greater than 3 mm is a useful first trimester marker for detecting fetal chromosomal abnormalities. The first trimester karyotyping has been performed in 1015 fetuses (Pandya 1995). The study reported that incidence of chromosomal abnormality increased with Nuchal Translucency thickness and maternal age.

The fetus with Nuchal Translucency thickness of 3 mm or more underwent CVS or aminocentesis and 18 fetuses were confirmed with the occurrence of Trisomy 21. Thus it has been proved that increase Nuchal Translucency thickness is an effective indicator of fetal aneuploidy (Taipale 1995). A multicentre screening study combined with maternal age has been carried out between 10 to 14 weeks of gestation for measurement of NT thickness (Pandya 1996). It was stated that out of 86 abnormal fetuses the NT thickness of 66 fetuses were found to be above 95% percentile. It was concluded from the screening study conducted in four fetal medical units in Greece, that the risk estimate for trisomy 21 based on fetal NT and maternal age has high efficiency (Theodoropoulos 1997).

A semi automatic measurement system using the sobel operator has been proposed to detect the border of NT (Bernardino 1988). However
reliable border evaluation of NT has not been achieved. Hyun-Mee Ryu et al (2006) observed that the measurement of NT increased with increasing Crown Rump Length (CRL) and the false positive rate increased with gestational age. The combined measurement of NT and NB in relation with Bi Parietal Diameter (BPD) provided a higher predictive value of 90% for detecting the DS in first trimester. (Piotr Sieroszewski 2006).

The sensitivity of measuring NT for screening DS is increased using three cut-off 2.5 mm, 3.0 mm and 95th percentile for each CRL compared with the fixed cut-off (Jae-Hyug 2006). It has been stated (Peter schmidt 2008) that NT measurement is not optimal even with profound training. A difference of 0.1mm or 0.2 mm in measurement leads to significant change in the risk assigned to the fetus and hence concluded that the NT measurements has to be precise. Yu-Bu-Lee et al (2007) presented a semi-automated detection procedure for measuring NT thickness based on Dynamic Programming (DP) improved by a nonlinear anisotropic diffusion filtering. The limitation of the proposed method is that it can be only applied when fetal position is as horizontal as possible.

Nasal bone hypoplasia during the first and second trimester has been associated with a high risk for trisomy 21 and has been suggested as a highly sensitive and specific sonographic marker for chromosomal aneuploidy. The first trimester ultrasound that determines the presence or absence of the nasal bone between 11 and 14 weeks of assessment of the fetal nasal bone was described by Cicero et al (2001) and detected 77% of Down syndrome cases.

Since the work reported by Cicero et al. (2001) regarding the association between absent Nasal Bones (NB) and Down syndrome, many studies have reported findings of an increased risk of fetal aneuploidies associated with failed ultrasonographic visualization of Nasal Bones. The
nasal bone length of fetus between 15 to 20 weeks of gestation were evaluated (Bryann Bromley 2002). The presence and size of the nasal bone have been considered to be the important markers in the detection of fetuses with DS in the second trimester.

Sonek et al (2003) proved that the analysis of nasal bone length measurements throughout gestation of different races (African - American and caucasian) were found to be the same. The fetal profile for nasal bone length of first trimester were examined (Cicero et al 2002) and the results reported did not have significant difference in the nasal bone length of the normal and abnormal fetus which measured only a few millimeters in length. The 3 Dimensional (3D) US performed for evaluating the fetal nasal bone as a sonographic marker of DS during the second trimester reported that the fetuses with non visualisation of nasal bone were considered as abnormal. (Wesley Lee et al 2002).

The recordings reported by Cicero et al (2003) concluded that for the detection of presence or absence of nasal bone, on an average of 80 scans were needed for an experienced sonographer to confirm the down syndrome affected fetuses during the screening of 11-12 weeks of gestation. The detection rate of DS fetuses were found to increase from 83% to 90% by including absent nasal bone to ultrasound aneuploidy markers (Anthony Vintzileos 2003). In a study performed by Zoppi et al (2003) on 5532 fetuses, there were 40 chromosomal abnormalities diagnosed and the nasal bones were absent in 70% of trisomy 21 cases. Comparison of nasal bone assessment by US examination at 11-14 weeks gestation and post mortem X-ray examination in fetuses with trisomy 21 were performed (Larose et al 2003). It has been reported that fetuses with absent nasal bone on US examination had NT thickness greater than 95th percentile.
The nasal bone was hypo plastic or absent in 12 of 19 fetuses with chromosomal abnormalities in a total of 1906 fetuses (Viora 2003). The reproducibility of the fetal nasal bone length measurement in the first trimester has been considered inadequate to conclude a DS fetus (Bekker 2004). Later Piotr Sieroszewski et al (2006) had evaluated the nasal bone length sonographically and concluded that including nasal bone length in the detection of DS increased the prediction rate.

According to Sonek et al (2006) the use of sonographic studies about absence or hypoplastic of the nasal bone in prenatal screening is strongly associated with trisomy 21. A prospective study on high risk thai population were performed on 407 fetuses. In euploid fetuses, the NBL increased with increasing gestational age (Bongkoch Naraphut 2006). Gabriele Tonni et al (2006) reported that if the nasal bone is absent NT should be measured and if it resulted in a higher risk then the karyotyping should be recommended for the mother. Minderrer et al (2003) revealed that the nasal bone has been absent under US examination but less distinct in physical inspection . It has been concluded that the fetal nasal bone should not distinguish between present or absent but between normal or hypoplastic.

Mehmet Tunc Canda and Namik Demir (2007) had reported first-trimester screening with ultrasound including nuchal thickness, nasal bone, tricuspid regurgitation, ductus venous blood flow and Fronto Maxillary Facial angle . The presence and absence of nasal bone increased the detection rate of DS to more than 95%. The contributions of nasal bone assessment in the first trimester among 1807 fetuses have revealed that 9 fetuses having Trisomy 21 (Recep Has 2008). The performance of first trimester screening for aneuploidies by including assessment of the fetal nasal bone in the combined test of maternal age, fetal Nuchal Translucency Thickness (NTT), Fetal Heart Rate (FHR) and serum free β-human Chorionic Gonadotropin (β-hCG) and
Pregnancy-Associated Plasma Protein-A (PAPP-A) were conducted by Kagan et al (2009).

The main objective of Min Chen et al (2009) was to investigate the feasibility and reproducibility of measurements of nasal bone length using a three-dimensional (3D) ultrasound in the first trimester and concluded from the study that independent 3D measurement of nasal bone offered no additional advantages over 2 Dimensional (2D) sonography.

Prenatal sonographic studies in the first trimester have demonstrated that a significant proportion of fetuses with Trisomy 21 have a shorter maxillary length than euploid fetuses. The objective of the study conducted by Sonek et al (2004) was to investigate the potential value of the Fronto Maxillary Facial (FMF) angle in second-trimester ultrasound screening for trisomy 21. It was concluded that the FMF angle was substantially higher in trisomy 21 than euploid fetuses. It has been reported that the FMF angle measured in normal fetus is less when compared with the DS affected babies (Sonek 2007). Molina et al (2008) have measured the FMF angle using 3D volumes of the fetal image. The results reveal that in the majority of second-trimester fetuses with Trisomy 21 the FMF angle is increased. Borenstein et al (2007) have reported that Trisomy 21 is associated with a flat face which can be quantified by the measurement of the Fronto Maxillary Facial angle. It can be observed from the discussions that the inclusion of FMF angle in the screening will increase the detection rate of DS from 90% to 94%.

The individuals with Down Syndrome have an unusually flat face (Down 1866). The nasal bridge is very short in such fetuses. Hence the Naso Frontal Angle of fetuses with DS is expected to show more variation from the NFA of the normal fetuses. Guis (1995) has manually measured the NFA and reported that there is no significant difference in the Naso Frontal Angle of
normal and abnormal fetuses. So far no automatic or semiautomatic algorithm has been reported for the measurement of NFA.

Analysis of US fetal images requires a considerable amount of user interpretation. Physicians are forced to make a manual segmentation of US features of fetal images to extract the interesting data. This manual approach presents several problems and is more tedious for the physicians. Interesting data like area and standard deviation have not been extracted accurately from the reproduced images (O’Leary 2002). Mignotte (2001) used a statistical external energy in a discrete active contour for segmentation of US images with significant noise and missing boundaries.

Segmentation of digitized medical images is needed for applications involving estimation of contour of an object, classification of tissue abnormalities, shape analysis, contour detection and texture segmentation (Guafong 2002). Despite the existence of several techniques, segmentation of specific medical images still remains a major problem due to the nature of US images (Fu-Yuan 2004). In the last decade, there is an increasing emphasis for analysing and processing images with statistical techniques. Klinger et al (1998) presented a morphological based classical mathematical approach for the segmentation of echocardiographic images. An automated fuzzy C-mean clustering algorithm has been described for image segmentation (Sahaphong and Hiransa Kolwong 2007). A fuzzy multiscale edge detection method has been developed using wavelet transform for endo and epi cardial border detection (Setarehdan 1999). Wolf et al (2002) described a semiautomatic segmentation method for 2D and 3D echocardiography data.

Kass et al (1998) stated that the user can derive a special snake or external force modification in order to attract the snake into boundaries of an interest by an iterative process. Finite element method is used to calculate the

Neuenschwande et al (1997) proposed a zip lock snake that acts as a growing snake; it does not need any initial contour. However it is limited in application as it is very sensitive to noise near the contour. Yu and Acton (2002) developed a two step semi automatic active contour based segmentation algorithm. Lai et al (1995) proposed a deformable contour model which is inappropriate for detecting soft tissue such as the intima-media layer. Initial contour procedure may lead to wrong results since the real images contain some noise in the artery lumen occasionally (Yuen 1999). Numerous researchers have applied and modified the snake technique for edge detection, pattern recognition, motion tracking and salient extraction via an energy minimization process (Melnerney and Terzopoulos 1996). The of Heitz et al (1994) proposed the Multiscale optimization strategy algorithm to perform the energy minimization process.

The Matched Filter algorithm given by Detmer et al (1990) indicates that there is a cross-correlation between a reference profile with the intensity profile in the direction perpendicular to the boundary. Barrett and Mortensedn (1996) in ‘Interactive live-wire boundary extraction’ have detected the edges using graph search algorithm. A few researchers have also used metrics based on distance between boundaries for their evaluation (Geiser 1990). DeGraaf et al (1992) used a metric based on the number of edge operations performed on the segmentation results. Muzzolini et al (1993)

Mishra et al (2003) proposed an active contour solution where the optimization technique is performed using a genetic algorithm. Corsi et al (2002) presented a level set based segmentation approach for real time 3D echocardiography data. The segmentation technique was devised to track the progression of ulcerated plaque using balloon modelling technique (Gill 2000, Mao 2000).


B-Spline snake algorithm for segmentation of fetal cardiac images has been proposed by Tauber et al (2004). The limitation of this method is that significant number of parameters are to be fixed by the user and hence leading to high inter-operator variations and also requires trained professionals to overlook the entire process. Visual Index based segmentation scheme for features has been proposed by Zhang Tinaxu et al (1996) for possible image segmentation. But the robustness of the algorithm in the presence of noise is not validated.

Segmented images consisting of texture and non texture regions based on local spectral histograms have been reported by Xiuwen Liu and Delia Wang (2006). This method has been proved to provide accurate
segmentation results on the test images. But, as the window size is too small, the variation within the same texture becomes large leading to inaccurate segmentation of features. Ultrasound image segmentation using morphological operators imposing Gaussian constraints were reported by Infantose et al (2008). The drawback of this algorithm is the inclusion of nearby areas having gray-levels similar to the region of interest in aliasing of the features.

Ashish Thakur et al (2005) proposed a region based segmentation of ultrasound B-mode breast and liver images using local statistics. A fairly classic approach for blood vessels segmentation in ultrasound datasets using model based region growing algorithm has been reported by Hold et al (2007). Although this algorithm runs faster, the reliability and reproducibility of the features segmented depends upon the seed pixel fixed and the estimated threshold.

Maroulisa et al (2005) have proposed a Variable Background Active contour model and applied it for the detection of thyroid nodules in ultrasound images. The results of the experimental study lead to the conclusion that the proposed model provides improved accuracy and is important due to the fact that nodule size and shape are factors affecting the subsequent nodule classification. Caiani et al (2006) developed a new method for nearly-automated Common Carotid Artery (CCA) contour detection by combining Seeded Region Growing (SRG) and Level-Set (LS) methods. This method is able to reliably detect the CA lumen compatibly with image quality.

Isil and Erdem (1997) examined the ultrasound image sequences of fetus head for the bi-parietal diameter measurement. However the computation time required for processing is not acceptable for real time applications. Also the number of sequences tested is limited in number because of the difficulties of acquisition process.

The literature review made in the context of sonographic soft markers for DS detection shows that the estimation of these fetal parameters in the first and second trimester of pregnancy is expected to detect the fetuses with DS. In the few articles the Nuchal Translucency region has been segmented and its thickness has been evaluated.

The semiautomatic or automatic segmentation schemes developed for various environments and applications require either a predefined template for unsupervised deformation using mathematical model or a prior knowledge, unique in terms of shape or contours that reflect specific region property which is then used to form a smooth contour. Unless a common method for contour estimation of various DS soft markers exists, the implementation of a MDSS for US fetal image analysis for DS detection may not be possible. Mostly the measurements of NT thickness, Nasal bone length and FMF angle have been carried out manually. Except in certain implementation wherein the NT thickness has been mentioned using automatic and semiautomatic segmentation algorithm. Due to the presence of speckle noise ,the anatomical structure of nasal bone, frontal bone and palate and other constraints establishing the general automatic or semiautomatic segmentation scheme for the estimation of NT, NBL, FMF angle and NFA is difficult and yet not been reported. Therefore the implementation of MDSS for US fetal images for DS detection requires basically a general processing
schemes followed by a reliable method to extract the contours of nasal bone, frontal bone and palate for the estimation of NT, NBL, FMF angle and NFA. A decision making module that facilitate automatic identification of DS category is required.

For objective decision making regarding the DS category, a neural network module have been developed (Gregony 1999, Maurer and Porenta 1999, Brijesh Verma 2001, Ibraheim 2006). A neural networks classifier classifies the subjects as normal and abnormal based on the evaluation of the soft markers. The Multilayer Back Propagation Network (MBPN) further identifies the nature of the pathology and outputs the category as normal and Down syndrome subjects.

As mentioned earlier, the major constraint in US fetal image analysis is the presence of speckle noise. The noise hinders the process of segmentation of NT region, nasal bone, frontal bone and palate. Hence the extraction of these regions is not possible. This motivated the research on US fetal image analysis for identifying a reliable segmentation scheme and implementing the MDS system.

In the present investigation, the limitations of the existing works have been considered for developing an improved identification system. The contour extraction and Neural Networks (NN) techniques have been used to segment the fetal soft markers and classify the subjects.

1.3 OBJECTIVES

The objectives of the research work are:

- To segment and estimate the chosen soft markers
  Nuchal Translucency Thickness
  Nasal Bone Length
Fronto Maxillary Facial Angle  
Naso Frontal Angle

- To compare and validate the estimated features for developing decision support system
- To classify the subjects into normal and abnormal
- To develop a MDSS to recognize the pathology.

The prime focus of this thesis is to realize a MDS system that classifies the input Ultrasound fetal images as normal and Down Syndrome subjects. The system facilitates the objectives and helps the medical experts as secondary observer for making unbiased diagnosis on Ultrasound fetal images for Down Syndrome detection.

1.3.1 Medical Decision Support System Implementation

The MDS system is developed with three prime focuses for its implementation to detect the specific kind of abnormality and shown in Figure 1.1.

a) General processing techniques include
   - Image acquisition and digitization
   - Image quality verification and re acquisition

b) Preprocessing algorithms for segmentation of anatomical structures comprise of
   - Filtering for speckle reduction
   - Selection of region of interest
c) Analysis aimed at solving a particular task or application. This step includes the following:

- Boundary extraction
- Classification by Neural Network Decision Support System
- Applications.

![Flow Diagram of MDS System for fetal Image analysis](image-url)

**Figure 1.1 Flow Diagram of MDS System for fetal Image analysis**
The images acquired by using ultrasound scanning system are given as input to the developed MDS system. In general processing the acquired image is verified for the prominent visibility of anatomical structure. The image is reacquired until the physician gets convinced with the quality. As general processing is mostly concerned with the acquisition system and physician decision where in routine procedures are followed, the explanations and discussions are made extensively pertaining to pre-processing technique and analysis.

1.3.2 Examination Procedure

As a common procedure of US imaging,

i) Subjects are given no prior preparation, such as fasting or sedation.

ii) Subjects are instructed to remove any articles of clothing or ornaments surrounding the area to be imaged. In some cases the patients may be asked to wear a gown.

iii) Subjects are positioned with face up by the physician on an examination table that can be tilted or moved. A clear gel is applied to the area of interest.

iv) The physician then places the transducer into contact with the skin and eliminates air pockets between the transducer and the skin.

v) The physician then presses the transducer against the skin and sweeps it back and forth to image the area of interest. The subject is simply required to relax and stay calm during examination.

vi) Once the procedure has been completed, the gel will be wiped off.
1.4 CHROMOSOMAL BASIS OF DOWN SYNDROME

1.4.1 Down Syndrome

Down syndrome, Down's syndrome or Trisomy 21 is a chromosomal disorder caused by an error in cell division that results in the presence of an additional third chromosome in chromosome 21. Down syndrome is the most frequent genetic disorder causing mild to moderate mental retardation and associated medical problems. It occurs in all races and economic groups.

Down syndrome is associated with some impairment of cognitive ability and physical growth as well as facial appearance. Individuals with Down syndrome tend to have a lower than average cognitive ability, often ranging from mild to moderate developmental disabilities. A small number have severe to profound mental disability. The incidence of Down syndrome is estimated at 1 per 800 to 1,000 births (Hook 1982; Hook 1983).

The human body is made of cells; all cells contain chromosomes, structures that transmit genetic information. Each cell contains 22 pairs of chromosomes (called autosomes) that are the same in males and females. The remaining pair of chromosomes, the X- and Y-chromosomes, are not shaped similarly, and thus are not matched in the same way as the autosomes. When the reproductive cells, combine during fertilization, the fertilized egg thus formed contains 23 chromosome pairs. A fertilized egg that will develop into a female will contain 22 chromosomes and the XX pair as shown in Figure 1.2, whereas the fertilized egg that will develop into a male will contain chromosome pairs 1 through 22, and the XY pair as shown in Figure 1.3. When the fertilized egg contains extra material from chromosome number 21, it will result in Down syndrome. Figure 1.4 shows the occurrence of Down syndrome due to a copy of Y chromosome in chromosome pair 21.
Figure 1.2  Normal Chromosomes (Female)

Figure 1.3  Normal Chromosomes (Male)

Figure 1.4  Abnormal Chromosomal structure (Trisomy21)
1.4.2 Characteristics of Down Syndrome

There are estimated to be over 100 characteristics of Down syndrome. Common characteristics of Down syndrome include:

- A flat facial profile
- An upward slant to the eye
- A short neck
- Abnormally shaped ears
- White spots on the iris of the eye (called Brushfield spots)
- A single, deep transverse crease on the palm of the hand
- Exaggerated space between the first and second toe
- Poor muscle tone (called hypotonia)
- Joint looseness
- Broad feet with short toes
- Learning disabilities.

Figure 1.5 shows the facial characteristics of babies with Down syndrome.

![Figure 1.5 Babies with down syndrome](image-url)
1.4.3 Down Syndrome Associated Medical Disorders

Congenital hypothyroidism, characterized by a reduced basal metabolism, an enlargement of the thyroid gland, and disturbances in the autonomic nervous system, occurs slightly more frequently in babies with Down syndrome. Several other well-known medical conditions, including hearing loss, congenital heart disease, and vision disorders, are more prevalent among those with Down syndrome.

About 66 to 89% of children with Down syndrome have a hearing loss of greater than 15 to 20 decibels in at least one ear, due to the fact that the external ear and the bones of the middle and inner ear may develop differently in children with Down syndrome (Mazzoni 1994). In addition to hearing disorders, visual problems also may be present early in life. Cataracts occur in approximately 3% of children with Down syndrome, but can be surgically removed.

Babies with Down syndrome often have hypotonic or poor muscle tone. Hypotonia may affect the muscles of the digestive system, in which case constipation may be a problem. Atlantoaxial instability, a malformation of the upper part of the spine located under the base of the skull, is present in some individuals with Down syndrome.

Approximately half of the children with Down syndrome have congenital heart disease and associated early onset of pulmonary hypertension, or high blood pressure in the lungs (Durmowicz 2001). It has also been reported that Down syndrome causes Alzheimer’s disease and 15 to 20 times higher risk of leukemia. Leukemia and leukemoid reactions show increased incidence in Down syndrome (Fong and Brodeur 1987).

Seizure disorders, though less prevalent than some of the other associated medical conditions, still affect between 5 and 13% of individuals
with Down syndrome. There is an unusually high incidence of infantile spasms or seizures in children less than one year of age, some of which are precipitated by neonatal complications and infections and cardiovascular disease (Korenberg 1992 and Delabar 1993).

1.4.4 Impact of Down Syndrome in Maternal Age

Researchers have established that the likelihood that a reproductive cell will contain an extra copy of chromosome 21 increases dramatically as a woman ages. Therefore, an older mother is more likely than a younger mother to have a baby with Down syndrome. Only about nine percent of total pregnancies occur in women 35 years or older each year, but about 25% of babies with Down syndrome are born to women in this age group. Table 1.1 shows the relationship between the incidence of Down syndrome and age of the mother.

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<th>Age of the mother</th>
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<td>Under 30</td>
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The incidence of Down syndrome rises with increasing maternal age (Penrose 1933). The likelihood that a woman under 30 who becomes pregnant will have a baby with Down syndrome is less than 1 in 1,000, but the chance of having a baby with Down syndrome increases to 1 in 400 for women who become pregnant at age 35. The likelihood of Down syndrome continues to increase as a woman ages, so that by age 42, the chance is 1 in 60 that a pregnant woman will have a baby with Down syndrome, and by age 49, the chance is 1 in 12. The incidence of Down syndrome in major countries of the world is given in Figure 1.6.

![Figure 1.6 Incidence of Down syndrome across the world](image)

Down syndrome diagnosis can be made during prenatal testing. A diagnosis can also be made shortly after birth. In this case, the doctor may suspect that a baby has Down Syndrome based on the presence of possible characteristics of the condition. A Down Syndrome diagnosis is confirmed with a special blood test.
Prenatal screening test for Down syndrome includes:

1. Multiple marker screening test
2. Maternal blood screening test
3. Triple screen
4. Quad screen

This screening test suggests an increased likelihood of Down syndrome and can be used for Down syndrome diagnosis.

1.5 DIAGNOSIS FOR DOWN SYNDROME

Tests used to diagnose Down syndrome are:

1. Amniocentesis
2. Chorionic Villus Sampling (CVS)
3. Percutaneous Umbilical Blood Sampling (PUBS)

1.5.1 Amniocentesis

In amniocentesis, a sample of the fluid surrounding the fetus is withdrawn. Fetal cells in the fluid are then examined for chromosomal abnormalities. A needle is usually inserted through the mother's abdominal wall through the wall of the uterus into the amniotic sac. After the amniotic fluid is extracted, the fetal cells are separated from it. The cells are grown in a culture medium, then fixed and stained. Under a microscope the chromosomes are examined for abnormalities. The most common abnormalities detected are Down syndrome, Edward syndrome (Trisomy 18) and Turner syndrome (Monosomy X). Amniocentesis is most safely performed after the 14th -16th week of pregnancy. Studies from the 1970's
originally estimated the risk of amniocentesis-related miscarriage at around 1 in 200 (0.5%).

1.5.2 Chorionic Villus Sampling

Chorionic Villus Sampling, conducted at 9 to 11 weeks of pregnancy, involves extracting a tiny amount of chorionic villi, tissue extensions that will eventually develop into a placenta. The tissue can be tested for the presence of extra material from chromosome 21. The villi can be obtained through the pregnant woman's abdomen or cervix. This type of sampling carries a 1-2% risk of miscarriage.

1.5.3 Percutaneous Umbilical Blood Sampling

The third diagnostic method, Percutaneous Umbilical Blood Sampling or PUBS, is the most accurate method and can be used to confirm the results of CVS or amniocentesis. However, PUBS cannot be performed until later in the pregnancy, during the 18th to 22nd weeks, and has the greatest risk of miscarriage.

PUBS are similar to amniocentesis, but instead of sampling the amniotic fluid which surrounds the fetus, PUBS examines fetal blood. PUBS testing have a turnaround time of about 72 hours and can detect chromosomal abnormalities, blood disorder, some metabolic disorders, infections, and some causes of structural problems. Miscarriage is the primary risk associated with PUBS and occurs in 1-2% of procedures. Additional possible complications are similar to those for amniocentesis and include blood loss at the puncture site, infection and premature rupture of membranes.
1.6 ORGANIZATION OF THE THESIS

The thesis is organized as follows:

Chapter 1 gives a brief introduction about the work undertaken. The existing works related to Ultrasound fetal images have been reviewed to understand the limitations and further extension required to develop Medical Decision Support system has been provided.

Chapter 2 deals with the measurement of NT thickness using the developed image processing technique. The preprocessing procedure used in this technique includes filtering, selection of Region of Interest (ROI) and segmentation of NT region. The results obtained are also presented.

Chapter 3 provides the extraction of contour of Nasal bone region for the measurement of NB length using Mean shift segmentation algorithm. The results obtained from the present investigation are provided.

Chapter 4 deals with measurement of FMF angle and NFA for the detection of DS. The segmentation results are also provided.

Chapter 5 presents the MDSS using neural network technique and its applications in automated classification of fetal images. The classification efficiency of the developed system is compared with MBPN and physician interpretation.

Chapter 6 provides the conclusion based on the results obtained from the segmentation of fetal parameters and classification. The future scope of the work to be carried out for improving the performance is also stated.