REVIEW OF LITERATURE

ANXEIY DISORDERS-

Anxiety has long been recognized as a prominent symptom of many psychiatric disorders. Anxiety and depression often occur together and, until the last part of the 19th century, anxiety disorders were not classified separately from other mood disorders. It was Freud (1895 b) who first suggested that cases with mainly anxiety symptoms should be separated under name of “Anxiety Neurosis”.

During 1970s, three anxiety disorders were recognized and were considered to be under the rubric of “phobia neurosis”, “Obsessional neurosis” and “anxiety neurosis” which include “panic attack”. The anxiety disorders reported to be underwent significant diagnostic reversion with the publication of DSM-III (American-psychiatric Association, 1980; Frances et al, 1993; Zal, 1988). The revised fourth edition of diagnostic and statistical manual of mental disorder (DSM-IV-TR) devised anxiety disorders into following groups.

- Generalized Anxiety Disorder (GAD)
- Obsessive-Compulsive Disorder
- Post traumatic stress Disorder
- Panic disorder without agoraphobia or with agoraphobia
- Simple/specific phobia and Social phobia

Anxiety both as symptoms and a syndrome is frequently reported by children and adolescent. Community based studies have found that anxiety disorders are to be one of the most prevalent psychiatric disorders (Kashani and Orvaschel 1990, 1988).

In one sample of 14-16 years old people the prevalence rate was 17.3%. All were showing a sufficient number of symptoms to meet criteria for an anxiety disorders. (Kashani and Orvaschel, 1988). Other estimates of anxiety disorder prevalence include 8.9% of 7 to 11 years children in a pediatric primary case setting. (Costello et al., 1988).
It has been established that anxiety disorders aggregate in families (Marks, 1986). Weissman et al. (1984) reported that the children of panic disorder proband to be are at an increased risk for anxiety disorders. The heritability estimates for a number of adult's anxiety disorders were reported by Kendler et al., (1986).

The high prevalence rates of anxiety disorders in the first degree relatives of affected people as compared to controls, were determined. A heritability of 0.43 was calculated from a family study by Tambs (1991). Two other population based samples on a combination family/twin study, generated heritability estimates ranging from approximately 0.20 to 0.35 (Jardine et al., 1984; Tambs and Mourn, 1993) within 8 to 16 years old range. (Topolski et al., 1997) recently determined that the heritability in anxiety disorders ranged 0.23 to 0.45 for males and 0.42 to 0.57 for females.

The majority of studies have been in agreement that there exists a genetic predisposition to anxiety at both clinical and sub clinical levels (Jardine et al., 1984; Kendler et al., 1986, 1992). The family studies demonstrate the possibility of genetic transmission but environmental exposure tends to vary with degree of genetic similarity.

In a review of five population studies conducted in the United Kingdom and Sweden prior to the development of any comprehensive specific criteria it was found that anxiety states were fairly common (about 2% to 4.7%) and more prevalent in women as compared to men between 16 to 40 years of age.

These epidemiological studies are very informative because they gather data from large number of subjects, statistical techniques and survey community samples of patients who are not under treatment. The study of large number of samples allows comparison across relevant groups on the basis of differences.

The principal psychological theory of panic disorder and its association with agoraphobia is the fear of hypothesis (Goldstein and Chambless, 1978). The theory suggests that agoraphobia is not a fear of public places but a fear of having panic
attack in public. Panic disorder patients fear their own fear so actually is that they misinterpret physiological sensation (Clark, 1986). They ruminate about serious illness, both physical and mental (Hibbert, 1984). In this over concern they may amplify slight physical sensations into signs of impending disaster, which could then spiral into full blown panic.

Evidence of a genetic contribution to those anxiety disorders can certainly be found in the literature. The familial aggregation of all major subtypes of anxiety disorders has been well established. This review is to assemble and integrate the literature relating to genetic research into anxiety-disorders and the possible impact of genetic research in this area, because the genetics of anxiety disorders has been the subject of a number of reviews (Foley and Hay, 1992; Di Nardo et al., 1988, 1994; Silverman et al., 1996a, 1996b; Finn et al., 2003). Fears and phobias are relatively common in childhood (Merikangas, 2002; et al., 1996; Barrios et al., 1988, 1989) and both environmental and genetic theories have tried to explain the etiology behind these conditions (Lichtstein et al. 2000).

Genetic epidemiological studies have documented that these disorders are familial and moderately heritable. Linkage studies have implicated several chromosomal regions that may harbor susceptibility genes. Increasing evidence from family and genetic studies suggest that genes underlying these disorders overlap and transcend diagnostic boundaries. Heritable forms of anxious temperament, anxiety related personality traits and neuroimaging assays of fear circuitry may represent intermediate phenotypes that predispose to panic and phobic disorders (Smaller et al. 2008).

Anxiety and depression symptoms in children and adolescents have been shown to be heritable and are also highly correlated. Furthermore, there have been indications in the literature of sex and age differences in the etiology. These studies set out to ascertain that to what extent, the genetic and environmental factors that influence anxiety symptoms in adults also influence symptoms and whether, these are the same in children and adolescents and males and females. (Eley, 1999; et al., 1997; Ginsberg et al., 1997b; last et al., 1987, 1992; Merikangas et al., 2000).
It is represented that women have higher levels of neuroticism and twice the risk of life time generalized anxiety disorders of men, gender specific effects were also explored (Hettema et al. 2004). Panic disorder and phobic anxiety disorders are common disorders that are often chronic and disabling, genetic epidemiologic studies have documented that these disorders are familial and moderately heritable (Smoller, 2008).

**CHROMOSOMAL AND MOLECULAR GENETICS OF ANXIETY**

Community surveys have shown that many of the anxiety disorders are amongst the most common of the psychiatric disorder, and that they cause extensive suffering and interference with work and social functioning. Anxiety disorders and fears are also considered as the genetic disorder (Marks, 1986; Smaller et al., 2000).

Molecular genetic studies of anxiety disorders also have not yet got much success. In part, this may be attributed to obstacles that complicate effort to identify genes for any complex disorder of non-Mendelian inheritance pattern which shows, genetic heterogeneity, incomplete penetrance and variable expressivity (Lander et al. 1994). The success in psychiatric genetics may require the development of a "genetic nosology" that can classify individuals in term of the heritable aspect of psychopathology (Smoller et al., 1998).

Linkage study of panic and phobic anxiety disorders have implicated several chromosomal regions that may harbor susceptibility genes; however, candidate gene association studies have not established a role for any specific loci to date. Increasing evidence from family and genetic studies suggest that genes underlying these disorders overlap and transcend diagnostic boundaries. Heritable forms of anxious temperament anxiety related personality trait and neuroimaging assay of fear circuitry may represent intermediate phenotypes that predispose to panic and phobic disorders (Smoller, 2008).

The structure of genetic environmental risk factors for anxiety disorders in men and women exhibit high levels of life time comorbidity with agoraphobia, specific phobia and social phobia (Hettema,
According to Gelernter (2001) several anxiety disorders segregate in the families. A duplication of part of chromosome 15q, apparently inherited in a non Mendelian fashion, has been found to be strong associated with phobic disorders. This usual genetic mechanism may partly explain the heritability of phobia and other complex traits (Flint, 2003). Gratacos (2001) identified an interstitial duplication of human chromosome 15q24-16q26 (named DUP25), which is significantly associated with panic/agoraphobia/social phobia/joint laxity in families and with panic disorder in non-familial cases. Mosaicism, (different forms of DUP25 within the same family), and absence of segregation of 15q24-26 markers with DUP25 and the psychiatric phenotypes suggest non Mendelian mechanism of disease-causing mutation (Gratocos et al. 2001).

The polymorphic region 5HTTLPR of the SLC6A4 gene was examined in relation to phobic anxiety and cognitive function. Sixty four community dwelling older adults were genotyped for the 5HTTLPR polymorphism to examine whether late life phobias are associated with the short(s) allele and whether cognitive impairment may precipitate phobic behaviors in association with the s-allele (Schultz et al. 2005).

TWIN STUDY OF ANXETY DISORDER

Twin and family studies have demonstrated that anxiety disorder can be influenced by genetic factors (Weissman et al, 1995; Mannuzza et al., 1995, Kendler et al., 1992, 1993, 1995). Because investigations have relied on the DSM system to definite anxiety disorder, phenotype suggest that the standard clinical nosology has been useful for genetic studies: it has described anxiety syndromes that demonstrate familiality and heritability. There has been a substantial amount of supporting evidence suggesting the potential usefulness of a biological approach. Slater and Shields (1969) examined a large unselected series of twins and found a concordance rate for anxiety neurosis of 50% for monozygotic (MZ) twins and only 4% for dizygotic (DZ) twin. Leder and Weing (1966) also showed that monozygotic were
more similar than dizygotic twins in their rate of habituation to repeated stimulation. Kelly 1980, Young, Fenton & Leder, 1980; Stein et al. 1999 suggest a genetic inheritability for anxiety and hysterical personality, irrational fears and their associated phobias. Epidemiological studies suggest sex differences in prevalence and twin studies report significant genetic effect. Studies of the genetic architecture of fear conditioning may inform gene-finding strategies for anxiety disorder.

The largest and most informative twin study of anxiety disorder to date has been done by Kendler and colleagues, who studied a population based sample of 1033 female twin pairs, this study has provided estimates of the heritability of DSM-III-R Agoraphobia (39%), animal phobia 32% and social phobia 30%, that suggest a genetic influence on the expression of the phenotypes, although environmental factors play a large role (Kendler al 1992; 1993; 1995).

Biological hypothesis of the pathogenesis of anxiety derived from pharmacotherapy and the relevant findings from genetic studies (twin and family studies) and molecular genetic studies (Domschke, 2007; Carrey et al., 1981a). Twin and family studies have indicated that genes influence susceptibility to phobic anxiety and panic disorder but the location of genes involved remains unknown.

STUDIES ON PHOBIAS-

Phobias are relatively common in the general population. An extensive survey found a rate of 5.9 phobias per 100 people with women having a substantially higher rate 8.0 than man, 3.4 (Myers et al. 1984). A phobia must also be distinguished from a fear or anxiety. Agoraphobia appears to be the most frequent phobia (Agras et. al. 1969). Costello (1982) studied fears and phobias in women only and found that 74% of the women reported having one or more fears. In contrast, situational phobias seem to have little or no genetic component (Smaller, 1998). In a subset of the sample, blood injury phobias resembled situational phobias in having greater evidence for environmental than genetic etiology, although familial aggregation of blood injury fears appeared to be due mainly to additive genetic factors (Neale et. al., 1994).
Many people have turned to the brain in order to understand the biological circuitry behind phobias. The amygdala, an almond-shaped nuclear complex located in the dorsal mechanical portion of the temporal lobe, has been proved to be intricately tied in with the brain’s perception of fear. A portion of the amygdala known as the lateral nucleus is particularly responsible for fear responses. The amygdala receives efferent projections from such areas as the olfactory system, the hypothalamus, the cerebral cortex, and the brain stem. It projects efferent signal to the dorsal thalamus, the cerebral cortex, and brain stem. There are many more circuits from the amygdala to the prefrontal cortex than the other way around, causing us to have so little control over our fears (Adolphs et al., 1995; Davis 1998; Garcia et al., 1994; La bar et al., 1998).

Le Doux (1998) proposed a hypothesis regarding lesions of the amygdala central nucleus interfere with energy measure of controlled fear including physiological and behavioral responses. There is evidence that amygdala and hypothalamic damage may be the cause of phobias. For instance phobic children are born with a decrease in the activation of neurons in their amygdala and hypothalamic region. Anomalies in the hippocampus and prefrontal cortexes may also be the cause of phobia. Damage to the hippocampus has a strong effect on memory, and thus could cause an individual to incorrectly remember a fearful event. The prefrontal cortex is associated with the phenomenon of extinction, the weakening of a fear response to a conditioned stimulus over time. Thus, damage to this region could allow for the persistence of a fear response for years after an initial encounter with stimulus. (Miranda White, 2002).

Bienvenu (2007) and colleagues examine twin heritability personality dimension, neuroticism and introversion that have been implicated in both axis I anxiety/depressive disorder and axis II disorders. They asked to what extent the genetic and environmental influences on neuroticism and introversion overlap with those underlying three phobias social phobia, agoraphobia, and animal phobia, they found that social phobia and agoraphobia were associated with elevations in both neuroticism and introversion. They further found that the genetic determinants of
the personality traits entirely accounted for the genetic influences of social phobia and agoraphobia. In contrast, the genes influencing animal phobia appeared to be largely distinct from those influencing the personality traits and also suggesting that non-genetic factors contribute little to the relationship between personality and phobic disorders. (Smaller, 2007).

These findings have several implications for understanding of the structure of phobia disorder. First, they help validate the nosologic hypothesis that all phobias are not alike. The etiology of specific phobias (e.g., animal phobia) is distinct from that of social and agoraphobia. Second, they highlight the importance of introversion, a trait that has received less attention than neuroticism in genetic studies and clinical research on anxiety. Studies aimed at identifying susceptibility genes for anxiety disorders have often used neuroticism as an intermediate phenotype. These results suggest that a parallel effort is warranted to identify the specific gene underlying introversion. Third and related implication is that personality traits are an appropriate target for researchers interested in the genetic basis of social phobia and agoraphobia since the underlying genes may be identical. From an orthodological standpoint, quantitative phenotypes may be preferred because they provide more power and reduce the risk of misclassification that can arise in the analysis of binary categories (Smaller, 2007).

TWIN STUDIES ON PHOBIA-

Several twin and family studies have suggested that major depression is genetically distinguishable from panic and phobic disorders (Weismann et al., 1993; Mannuzza et al., 1994; Beiderman et al., 1991; Kendler et al., 1993). Twin and adoption studies help address the question of whether the familial nature of phobic and panic disorders is due to genetic influences. By comparing concordance rate of monozygotic and dizygotic twins, one can estimate the heritability (proportion of phenotypes variance due to genetic factors) of these disorder. Although this estimate will vary depending on the population studied (Torgerson, 1983; Perna et al., 1997).
Situational-phobia (e.g., driving, flying, enclosed places) are more closely related to agoraphobia than are other specific phobia (Martin et al. 1997). The strongest history of all anxiety disorders is seen in blood injury phobia (Marks 1986; Scapira et al., 1970).

Family studies suggest that phobias are familial (Noyes et al. 1986; Fyer et al. 1990; 1993, 1995; Stein et al. 1998) and twin studies of self-report fears consistently suggest etiological rate for genetic factors (Torgerson, 1979; Rose et al. 1983; Rose & Ditto, 1983; Neal & Fulkar, 1984; Philips et al. 1987). Twin studies have also support a role of genetic factor in phobia subtype (Carey & Gottesman, 1981; Torgersen, 1983; Kendler et al. 1992a, 1999a, 2001a; Sure et al. 1993; Neal et al., 1992, 1994a). Most of the studies have consistently suggested important sex differences in the frequency of irrational fears and phobias (Bourdon et al. 1988; Kessler et al. 1994, Frederixon et al. 1996; Curtis et al. 1988), their critical presentation and their risk factors (Cameron & Hill, 1989; Weinstock, 1999; Turk et al. 2000; Shear et al. 2000). Twin studies clarify the impact of sex on both genetic and familial environmental risk factors (Kendler et al. 2002).

In school aged twins with a mean age of 7.6 years emotionality, tension and shyness were significantly more similar among MZ and DZ twins (O‘Conner et al. 1980). At the age of seven, MZ twin significantly more concordant than DZ twins for separation distress, emotional reactivity and being fearful and inhibited (Goldsmith & Gottesman, 1981). (Fyer et. al, 1995). Most of the earlier studies were based mainly on DSM-III (1980) DSM-III-R (1987) criteria for phobic disorders. The role of genetic factors in the etiology of phobias comes from one population-based sample of female twins. (Kendler et al., 2001). The objective of the study was to determine the genetic and environmental sources of individual differences in fear conditioning by means of twin sample (Hettema et al., 2003).

**AGORAPHOBIA**

Several studies have shown the nature, mode of inheritance prevalence etc. of agoraphobics. (Marks, 1969; Solyom, et. al 1974; Terhune, 1961). The common
impression is that the families of agoraphobics are characterized by parental, over protection and have shown support for this opinion by nothing a significant incidence of maternal overprotection. Terhune. (1961); Tucker, (1956), Parker (1979), examined differences in over protection for social phobic, agoraphobics and control Social phobic rated both parents, as low on care and high overprotection while agoraphobic scored their parents low on maternal care but were identical to control on rating an overprotection. Findings of low maternal care support the general consensus, with the exception of Buglass et al. (1977), that agoraphobic have a history of poor relationship with their parents. Shov and Parker( 1979), argued that these early experiences serve as a significant predisposing factor in the development of agoraphobia. In agoraphobic families the prevalence of psychiatric disorders is higher than in families of normal control.

Several studies seem to indicate that the fears of phobia run in families and are specially associated with mother and daughters (Agras et al. 1969; Goldstein and Cambless, 1978). The findings by other would appear to support this conclusion. Leibowitz and Klein (1979), reported that 20% outpatient and 50% impatient adult agoraphobics has a history of separation anxiety. Marks (1970) pointed out, some agoraphobics are active, social and outgoing before their symptoms begin. With the onset of panic attacks, they become increasingly anxious, afraid of venturing outside, dependent on others for support withdrawn, and so on. It seems likely, that most posses certain premorbid personality characteristics that contributed to the development of agoraphobia. Shafar (1976) reported that 83% of her samples of phobia 74% were agoraphobics. Similar findings have been reported by others (Brown & Kohout, 1979; Solyom et al. 1974; Weeks, 1978). Buglass et al. (1977) were also able to show that 25 of 30% agoraphobics could identify a correlation of events to the onset of their phobia.

Brown and Kohout (1979) found that 76% of those agoraphobics identifying a precipitating source said that rejection or loss in an interpersonal relationship was associated with the onset of their panic attack. Supporting evidence for the role of
physiological factors in the development of agoraphobia comes from the works of pits and McClure (1967).

These investigators found that agoraphobics may have been reliably produces panic attack symptoms in a majority of anxiety neurotics but not in normal. These results have been replicated by others. (Bonn, 1973; Fink et. al, 1969; Kelly et. al., 1971). The environmental experiences that predisposed to agoraphobia, social phobia, situational phobia and simple phobias were most important for agoraphobia and social phobia and relatively unimportant for the simple phobia and the genetic factor that predisposed to all phobias were most important for animal phobia and least for agoraphobia (Kendler et al., 1992).

In one of the direct interview family studies to examine the comorbidity of panic disorders and agoraphobia. Noyes et al. (1986) found that relatives of probands with agoraphobia were at increased risk of both agoraphobia and panic disorders while relatives of panic disorder probands had an increased risk of panic disorder but not agoraphobia. They interpreted the findings as consistent with the hypothesis that agoraphobia represents a more severe variant of panic disorder, but subsequent studies have produced conflicting results. (Mendlewicz et al., 1993; Goldstein et al., 1994).

Recent reports have also linked anxiety, panic states to cardiovascular disorders (e.g. Kelly, 1980). Specially found in young women in mitral valve prolapsed syndrome (MVPS). Kentor et.al (1980), compared with 25 agoraphobic women with a group of control for the presence of MVPS. They found that an extraordinary (44%) of the agoraphobic subjects and only (9%) of the controls had MVPS (Kentor et. al., 1980).

**GENETIC AND BIOLOGICAL FACTORS**

Many findings suggest that agoraphobia is a severe subtype of panic disorder, although this is not universally accepted (Villafiverte, 2003). According to Moran (1995) Agoraphobia is believe to run in families. With only modest evidence for a
genetic component, it is all the more surprising that the major cause of panic, agoraphobia and related anxiety disorders could lie almost entirely within the human genome. This appears to be because of bizarre twist in our DNA: an unprecedented common duplication of genetic material on chromosome 15 leading to three instead of two copies of about 60 genes in most cells. This is particularly interesting as panic and social phobias, have been regarded as some of the least heritable psychiatric disorders and molecular genetics has until now been unsuccessful in unrevealing the etiology. This unexpected a novel cause of psychiatric disorders could have fundamental implications for the cause of mental illness (David et al., 2002).

Kindler (2001) assessed the lifetime history of agoraphobia, social phobia, situational phobia as well as their associated irrational fears. According to Fyer et al. (1995), each of three DSM-III-R phobic disorders (Agoraphobia with panic attacks, specific phobia and social phobia) is familial and “breeds true”. The rates of each phobic disorder were considered in first-degree relatives of proband groups. With modest evidence for a genetic component, it was reported by Gratacos et al. (2001) that the major cause of panic, agoraphobia and related anxiety disorders could lie entirely within the human genome.

Describe result for panic disorder and agoraphobia which are closely related common, heritable anxiety disorders. It is the first complete linkage genome scan for agoraphobia. For agoraphobia, the most promising potential linkage was chromosome 3, found behavioral inhibition prevalent in the offspring of parents with panic disorder and agoraphobia. In the research examined the psychiatric correlates of behavioral inhibition by evaluating the sample of offspring of parents with panic disorder and agoraphobia. Findings indicate that inhibited children had increased risk for multiple anxieties, overanxious and phobic disorders. Much of knowledge of the role of genetic factors in the aetiology of phobias comes from population based sample of female twins. Kendler et. al., (2001) examine the source of individuals differences in the risk for phobias and their associated irrational fears in male twins.
SPECIFIC (SIMPLE) PHOBIA

Simple phobia is a common anxiety disorder and lifetime prevalence is 11.3% (Kessler et al., 1994), that often causes significant subjective distress and can also cause significant impairment (Magee et al., 1996). According to DSM-III-R diagnostic criteria (American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 3rd edn, revised. American Psychiatric Press: Washington, DC, 1987.), simple phobia is characterized by a persistent fear of a particular stimulus that at some point reliably provokes an anxiety response, either avoidance of the stimulus or endurance of the stimulus with intense anxiety, and the recognition that the fear is unreasonable.

There are unwarranted fears caused by the presence or anticipation of a specific object or situation. The most common source of these phobias are animals, heights, closed spaces, blood, injections etc. The majority of those phobias occur in woman and they very often begin in early childhood (Marks and Gelder, 1967). Agras et al. (1969) also showed how infrequently animal phobias seek help from professionals. In their sample, only 4% of the cases was severe enough to require attention. Among the general population, fears of animals and insects are much more frequent. In the sample of Agras et al. (1969), fear of snake was seen in 39% of the respondents.

In student population, the majority reported feeling mildly uncomfortable in the presence of non-poisonous snake, only 1-2% actively avoided snake (Marks, 1969), and also reported that nearly 95% of cases observed were women. This figure is accrued for post pubescent individual, before puberty, fear of animal are found commonly girls and boys (McFarlane, Allen, Hanzik, 1954; Marks & Gelder, 1967). Agras et al. (1969) found height and darkness phobic made up only 2% each of their sample. Simple phobia may not be a homogenous category however; Ost (1983) found that age of onset differed across four grouping of categories. According to Rachmann (1977), infants are especially prone to fears of loud noise and strangers. Similar findings were also found by Ost Hugdahl (1981), they include several phobia types. Ost, and Hugdahl (1984) analyzed their data separately for snake
phobics only and found that 50% reported that they had acquired their fears directly. Fyer et al. (1990) investigated the relatives of simple phobics. They demonstrated that simple phobia occurs in 31% of relatives of simple phobic probands compared with 11% of the relatives of controls. There was no difference in the rates of depression or other anxiety disorders.

Marks (1969) found that a majority of individuals who had simple phobic specific animal fears come from the age of 12 and that most considered their family life happy, only 20% described frequent parental quarrels. Phobias are associated in the same family has been addressed in several studies. Marks (1969) reported that only a small number of patient (5%) reported other immediate family members with the same phobia. Rimm et al. (1977) revealed similar finding. The majority of their subjects with specific phobias indicated that no other member of their immediate family shared their feared. These reports seem to suggest that modeling influences are insignificant for the majority of individuals with specific phobias. This conclusion does not agree with other reports showing relatively strong association between the fears of mothers and children (Agras et al., 1969; Hagman, 1932; John, 1941).

Marks (1969) found a dominant or over protective mother was reported by 15%. 10% indicated that the mother were nervous. It is likely that a control group would have reported 30% incidence of “nervous” mothers, especially considering the failure to adequately define the term nervous, nearly 50% reported that they had various fears. Other childhood experiences such as schooling were unremarkable. Marks (1969) found that 35% of the simple phobias he sample could be described as dependent and anxious.

GENETIC AND BIOLOGICAL FACTORS-

Recently, it has been suggested that situational specific phobias (e.g.: driving, flying, oceans etc.) are more closely related to agoraphobia than are other specific phobia type. Torgersen (1979) suggested that hereditary factors may influence the development of animal fear and other miscellaneous fears such as fire,
mountain, oceans, and bridges etc.) Gelernter et al., (2003), found that several anxiety disorders segregate in the families. The genetic and environmental influences on neuroticism and introversion overlap with those underlying three phobias -specific phobia, agoraphobia and social phobia. These are associated with elevations in both neuroticism and introversion. The gene influencing animal phobia appeared to be largely distinct from those influencing the personality traits. These findings have several implications for understanding of the structure of phobic disorders. Firstly, they help validate the nosology hypothesis that all phobias are not alike. The etiology of specific phobias is distinct from that of social phobia and agoraphobia. Secondly, they highlight the importance of introversion, a trait that has recovered far less attention than neuroticism in genetic studies and clinical research on anxiety disorders.

Phobias are familial phenotypes in which first degree relatives of those affected have significantly increased risk relatives to the general population risk (Villafuerte et al., 2002).

Genetic epidemiology studies have documented that the phobic anxiety disorders are familial and moderately heritable. Linkage studies have implicated several chromosomal regions that may harbor susceptibility genes; however, candidate gene association studies have not established a role for any specific loci to date. Increasing evidence from family and heritable forms of anxious temperament, anxiety related personality traits and neuroimaging assays of fear circuitry may represent intermediate phenotypes that predisposed to panic and phobic disorders. (Smoller et al., 2008).

TWIN STUDIES ON SPECIFIC PHOBIA-

Twin studies suggest that modest portion of the familial resemblance in anxiety is heritable (Gelernter, 2004). Twin studies conducted using self report questionnaires of fears have found moderate heritability (Rose and Ditto, 1983). The relative importance of genetic and environmental influences on specific phobias and fears, of animal, situational, and mutilation fears and phobias were established in
numerous families and twins pairs (Lichtenstein et al, 2000). The marker D14S75 were reported in the dominant model for simple phobia in the first genome scan linked study for simple phobia by Gelernter et al. (2003)

**SOCIAL PHOBIA**

Social Phobia is less coherent than Simple Phobia and Agoraphobia and tend to be intermediate to the two groups. Marks (1969), Agras et al.(1969), Amies et al., (1983) found a fear of social situations to be prevalent in the general population and unlike in the other phobia, the sexes are more evenly represented in social phobia, As will be recall 95% of simple phobics (i.e. animal phobics) are women by comparison 60% of a sample of social phobics were women Marks (1969). Greeberg et al. (1983) believe that patient with more generalized social anxiety should be classified as having avoidant personality disorder and restrict social phobia to patients with discrete or specific forms of performance or social anxiety.

Social phobia is a common anxiety disorder (Gelernter, 2004). Their goals were to ascertain the range of functional impairment attributable to social phobia in community sample and to verify the existence of social phobia subtypes in community (Stein, 2000). According to Rosa (2001) the risk of heavy drinking and alcohol abuse/dependence were prospectively assessed among individuals with DSM-III. Social phobia and individuals with sub clinical social phobia (irrational fear of social situations without significant impairment or avoidance). Evidence suggests increased cardiovascular risk and autonomic impairment among individuals with chronic anxiety. Additionally gender and age related cardiovascular profiles have not been examined in relation to social phobia (Grossman, 2001).

Findings from biological challenge and treatment studies can clarify the relationship of social phobia to panic disorders and agoraphobia (Pith et al. 1967). Weerts and Lang (1978) found that students fearful of spider to react with greater effect and greater change in heart rate to fear relevant scenes than did students fearful of public speaking. The anxiety disorders including social phobia are
common among older adults, very little is known about the epidemiology of social phobia in latter life. (Cairney et al., 2007).

Several controlled studies have also compared how adult social phobics, agoraphobics, simple phobics and normal controls retrospectively rate their parents, child rearing practices and attitudes. As a group, social phobics perceived their parents to have been less caring, more rejecting and overprotective as compared with normal controls (Aprindell et al., 1983). However, no contrasts were carried out among the phobic groups, so the specificity of these findings for social phobics is uncertain. These studies also suffer from the deficiencies inherent in retrospective assessment.

Current knowledge of neurobiology of social phobic and social anxiety is reviewed with the framework of chemical models of anxiety. Preliminary evidence for noradrenergic, serotonergic and adrenosinergic systems in the neurobiology of social phobia is presented (Uhde TW, 1994).

Epidemiological studies have suggested that social phobia is equally common in males and females (Marks and Gelder, 1966; Eolyom et al., 1986; Amies et al., 1983) and life time prevalence is estimated as 2.8% (Refier et al. 1988). According to Strauss (1993) social and simple phobia are present in the childhood stage of human being. The recent studies have addressed the overlap between avoidant personality disorder and generalized social phobia (Herbert et al. 1992; turner et al., 1992; Holt et al., 1992). These phobias are fairly common, with a lifetime prevalence of 2% (Myers et al., 1984) and though perhaps not of clinical proportions, many people experience significant discomfort in social situations (Zimbardo, 1977). Unlike other phobians which occurs in woman more frequently than in man, social phobia occurs about equally in the two sexes. Social phobia has a high comorbidity rate with other disorders and is often found in conjunction with generalized anxiety disorder (GAD), specific phobia panic disorder and OCD (Turner et al., 1990).
In spite of the fact that together with panic disorder and OCD, social phobia has a high descriptive validity and high degree of comorbidity, disorders with the highest rate of co-occurrence are agora phobia, simple phobia and OCD (Schneier et al., 1992).

In most studies reliability for social phobia has been reported. Dinardo et al. (1993) reported a Kappa Value of 0.79 for social phobia as a principal diagnosis. In a recent study in relatives of social phobia probands was found that social phobia (DSM-III-R) occurring was associated with 16% for social phobic but not for other anxiety disorder (Fyer et al., 1993). The social phobia prevalence, impairment, pattern of co-morbidity and other correlates of DSM-IV social phobia in adolescents and young adults, separating generalized and non generalized social phobia. Respondents with generalized social phobia reported an earlier age of onset, higher symptoms persistence more co-morbidity, more severe impairment indicated more frequently parental history of mental disorders than respondents with non generalized social phobia (Wittchen et al., 1999).

Behavioral electrophysiological and imaging studies have found evidence that anxiety disorders are associated with left hemisphere dysfunction higher than normal activation of right hemisphere regions. Few studies, however, have examined hemisphere symmetries of function of social phobia and the influence of comorbidity with depressive disorders unknown (Gerard et al., 2004).

GENETIC AND BIOLOGICAL FACTORS-

Few studies have been reported regarding the role of genetic and biological factor in the development of social phobias. Targer (1979) found that monozygotic (MZ) twin showed a higher incidence than dizygotic (DZ) twins of intra pair similarly in social fears, several anxiety disorders, including social phobia are genetically influenced.

Marks (1979), found that over 50% of one sample of social phobia indicated that they were fearful, timid, or overly shy as children, and after puberty, 45% were social isolates. These findings support the idea that most social phobics have a
history of social fears and avoidance of social situations prior to onset. It seems that most social phobic were at risk in childhood for developing the disorders.

In contrast to social fears, simple phobia, childhood, increase in frequency and show little decline during early and middle childhood (Rachman, 1974). Shepherd, et. al (1971) surveyed over thousands of people, found that their children’s fears of meeting new people and shyness as continuing into middle adolescence, whereas fears of darkness and animal diminished with age.

The familial relationship between social phobic and panic disorder remains uncertain. Relatives of probands with social phobia have been reported to have an increased risk of social phobia but not panic disorders (Fyer et al, 1993; 1995; 1996). However in one large family study, social phobia did aggregate in the relatives of probands with panic disorder (without comorbid social phobia). (Horwath et al., 1995), because this association was seen in relatives probands with and without panic disorders.

Social phobia aggregates in families and is genetically influenced. In studies of adult probands, social phobia has consistently been found to aggregate in their families including in their children. Moreover, a no. of social anxiety traits are enriched among first degree relatives of probands with social phobia. There is some evidence that the more severe, generalized subtypes of the disorder show the strongest tendency towards familial aggregation (Gelernter, 2004). According to Wittchen (1999) social phobia is higher in females than males and also describes prevalence, impairment patterns of comorbidity and other correlates of DSM-IV social phobia in adolescents and young adults separating generalized and non generalized social phobia.

Rimm and Lepebvre (1981) pointed out Genetic linkage analysis can provide the means to identify genomic locations harboring susceptibility loci for genetically influenced disorders. Identifying loci for social phobia for chromosome 16 markers was identified D16S415 and D16S503 under a model of recessive inheritance and additional areas of interest were identified on chromosomes 9, 14 and 18. These
finding meet conservative criteria for “suggestive” linkage. The gene encoding the norpinephrine transporter protein (SLC6A2) maps to this broad region, making SLC6A2 both a positional and physiological candidate for influencing social phobia risk. Social phobia was intermediate in that it was influenced by both environmental as well as genetic factors. A small role for shared environmental influences was observed owing to single common factor that accounted for less than 12% of total variance for any disorder (Hettema, 2005). This study suggests that social phobia aggregates independently of other phobic disorder such as agoraphobia or specific phobia (Gelernter, 2004).

TWIN STUDY ON SOCIAL PHOBIA-

Over the first year of life, the development of smiling and of fear of strangers was reported more similar among monozygotic (MZ) than among dizygotic (DZ) twins (Freedman, 1965). At the age of about 22 months, in interaction with a stranger but not with the mother, the degree of apprehension was found to be more similar among MZ than among DZ twins (Plomin & Rowe, 1979). Slightly older twins of age about 3.6 years, showed substantial genetic influences on their emotionality (Plomin & Rowe, 1977).

The genetic and environmental contribution to fear and fearfulness in adults has been investigated (Rose et al. 1981; Neal and Fulker (1984) and analyzed data on two fear factors “fear of social criticism and “fear of meeting people and of leadership,” obtained from twins and their parents. For these factors, the heritabilities were 0.46 and 0.45 respectively, heritability in males of the proportion of the variance of characteristic observed in a population that is attributable to genetic differences amongst individuals.
MATERIAL & METHOD

Behaviour genetics is a field in which variations among individuals are separated into genetic versus environmental components. The most common research methodologies are population studies; family studies i.e. closed relatives, sibships analysis, pedigree analysis etc. and the twin studies.

POPULATION STUDIES-

In population studies, prevalence and incidence rates of mental and other disorders derived from community based surveys have important scientific and health policy implication. Variations in such rates can provide clues to possible causes and can be used as base rates for corporative purpose in genetics.

In the present work therefore two types of samples were considered for the studies of different types of phobias. One sample was from the general population of Northern India (mix population of almost all types of available communities, considering that marriages are not confined type in this group). Another sample was from a large community i.e. Momin Ansar (Ansari) group where confined marriages (cousin marriages and marriages among relatives etc.) are quite common, this is considered as a volunteer or community group, the data were collected from these two streams and compared to study the effects of genetic factors, family environment (familial) and general environment on the incidence, age at onset, mode of inheritance and prevalence of different types of phobias.

FAMILY STUDIES

Pedigree Analysis

Children share 50 percent of their genes with each parent. Therefore genes to be influential what so ever, the trait in question must run in families. Running in the family is necessary though not sufficient condition for a trait to be genetic.

The family studies reveal the familial nature of a disease/disorder, its mode of inheritance, the range of clinical or phenotypic expression within the family and the intergenerational difference resulting from family dynamic genes
and environments. The classic family study design requires the collection of a large sample of cases or probands, followed by the systematic evaluation of relatives.

A proper collected family sample is valuable for many kinds of studies; studies of rates of illness among relatives can help to define the trait/disorder as heritable or non heritable, autosomal and sex linked and also its phenotypic spectrum i.e. recessiveness or dominance complete/incomplete penetrance, variable or full expressivity etc. Therefore, the subjects for the present study were informed about the goals of the study and a verbal consent prior to telephone interview was taken from every proband and his/her relatives, for face to face interview a written consent was taken (In most of the cases the interview was conducted face to face). A sum of 7420 participants from general population group and a total of 8436 respondents from community group were evaluated for three major phobias i.e. Agoraphobia, specific phobia and social phobia. Diagnostic information was obtain from probands and relatives of probands by a preceding semi-structured interview based questionnaire having a reliability of 0.7 (test retest).

Interviewing is of a central importance in medicine; it is a core skill in all medical practices and is arguably the core skill in clinical psychogenetics too. There is a meaningful distinction between interviews that are free form and those that are standardized, the later are either fully structured or semi-structured and specify to varying degrees the contents, order and wordings of the interview. Their reliability and validity can usually be specified as compared to free forms which are non-specific. We practiced in the study a semi structured diagnostic interview based on DSM-IV criteria. Every diagnostic interview includes an assessment of patients psychopathology including not only the formal mental status testings which may be conducted but also the inferences and conclusions which an interviewer draws as the interview is conducted. Besides the standard close ended question (of one word answer ‘yes’ or ‘no’), we also asked the open ended questions (the questions having narrative answers) to elicit the history of the
disorder by inviting the proband (and sufferer relatives) to give a narrative
description of the course and chronology of his or her symptoms i.e. how did the
disorder began, was the onset sudden or gradual, what was the age at onset? etc.
The information gathered in this way helped us not only to assess the presence or
absence of the phobic condition and its types but also the patients family, work,
setting, friends and other relationships which were affected by his or her illness.

The diagnosis of phobia type was also completed using the questionnaire
based on DSM-IV diagnostic criteria. All the patients chosen for the present
studies satisfied DSM-IV criteria for anxiety disorders. A proband was selected
and the questionnaire based on the DSM-IV (1994) diagnostic criteria
administered to the patients for confirming diagnosis. These probands and all
available first, second and third degree relatives were personally interviewed as far
as possible, using a selected format questionnaire having reliability 0.7 (test
retest). The informations was also collected from telephones and audiotapes for
the relatives who settled in other cities or for those whom only historical
information was available and when there was disagreement a consensus diagnosis
was made by two psychiatrists.

The diagnosis of all sufferers was made by two expert psychiatrists. On the
basis of the symptoms, severity and symptoms impact on quality of the life.
Associated disorders and behavioral patterns were also measured using the family
history, gender differences, developmental mile stone, education etc. Variable
related to illness and treatment (e.g.-age of onset, medication, rates of specific
symptoms and variable related to physical health) etc. were taken from each of the
subject separately and in detail. The questionnaire involved 19 items. If a fear of
situation or some object was reported, a series of questions was asked to ascertain
whether the fear met the criteria for phobic level response. If the participant
assured ‘no’ to all the phobic questions and mentioned that the fear did not
interfere with usual or routine life activities, the phobia status was not given to the
person however if the answer was not ‘no’ to all questions and the person
mentioned that the life was affected due to the avoidance behavior, a phobic status
was established and it was considered a sufferer case and was recorded at the phobic level. A phobic level response to one or more of the situations listed by diagnostic category in the tables resulted in a diagnosis of the phobic disorder type.

Appearance, psychomotor behavior, and to some extent emotional state could be judged through visual inspection during the interview. As far as possible every proband in both types of samples and his or her sufferer relative was contacted personally and besides interviewing we also showed them the pictures, paintings or photographs of the things and situations of which they were found to be afraid of (for example those who reported to be animal phobic the photographs of different insects, spiders, snakes, birds, lizards, mice, rats, lion, dogs etc were shown, painting showing the burning louses, injured people with bleeding wounds, were shown to the respondents of some specific and situational phobias etc to confirm whether the patients is having simple fear or that he/she was a confirmed phobic of those things or situations. Thus, these pictorial stimuli served as conditioned stimuli to provoke an irrational fear in the real phobic patients for further testing, by observing patients reactions and conditions i.e., sweating, pale faces, shivering, increased heart beats, fast pulse rate and deep heavy breathings etc we confirmed considerable number of cases for the presence or absence of the disorders, using this provoking conditional stimuli method.

Raw data from all available subjects were utilized; with the help of raw data pedigrees were constructed up to three or four generations (depending upon the availability) to draw the conclusions about the mode of inheritance and prevalence of the disorders.

The pedigree where females were the probands were represented as groups A, B, C, D, E and Q, R, S, T, U. Similarly the male proband pedigrees were represented as F, G, H, I, J and V, W, X, Y, Z groups in community and general samples respectively. These five groups in each category were constructed according to the type comorbidities observed for other psychoneurotic disorders among sufferers and non-sufferers relatives of the probands.
Attempts were also made to find out the possible causes of the disorders, age of onset, most vulnerable age groups symptomatology and the gender specific differences in the penetrance of the related gene/genes.

The present study aimed to assess:

1. Whether genetic or environmental effects are of similar magnitude in the etiology of phobic disorders in the volunteer and general population samples?
2. Whether the genetic risk factors are same in the two samples?
3. How much consistent are the results obtained across different diagnostic approaches to different phobia in the two samples (volunteer and general) separately.
4. Are the modes of inheritance, age of onset and prevalence, same for the major types of phobias or there are differences?
5. If there are differences what are the main reasons and factors of influence?
6. Is there any gender specific effect in the inheritance and prevalence of these disorders?
7. Are there quantitative differences in the role of genetic and environmental risk factors for irrational fears and phobias in males and females? Might the heritability of one phobia subtype be higher in males than females and vice versa?
8. Are there quantitative differences in these risk factors? That is could the genetic/or environmental influences on phobias in male differ from those which act on females?

To evaluate the above mentioned conditions we assessed the family history, the life history of every sufferer, the pedigree analysis calculating the phenotype ratio between sufferers and non sufferer’s relatives of probands. Sib ship analysis and the penetrance of genetic factors in the sibs and I, II, III, degree relatives of probands, and also the sufferers and non sufferers monozygotic and dizygotic twins of the two types of samples.
We asked more than 30 types of specific individual fears from the three major types of phobias (Agoraphobia, specific and social phobia; beside we also asked respondents “is there anything else you” have been unreasonably terrified to do or to be near? If any phobia described in responds to this question, best belonged with of any of these major forms, it was also considered.

A number of subjects reported having more than two types of phobias or a phobic condition with some other psychoneurotic disorders: such cases were covered under the comorbid status.

**SCREENING QUESTIONNAIRE FOR PHOBIA**

- Do you generally become afraid by specific situation or object? [ ]
- Do you generally avoid gatherings and crowded places? [ ]
- Do you generally feel that heart rate is increased in phobic situations? [ ]
- Do you feel suffocation because of fear? [ ]
- Do you feel so scared that your tongue gets dried up? [ ]
- Do you get trembling in sudden events? [ ]
- Do you feel that you will lose your presence of mind in phobic condition? [ ]
- Do you feel chest pain in phobic condition? [ ]
- Do you have feeling of choking in phobic condition? [ ]
- Do you feel physical weakness? [ ]
- Do you feel hot flushes in phobic condition? [ ]
- Do you feel that your mind is in numbness if you see serious events? [ ]
- Do you feel difficulty in respiration in phobic condition? [ ]
- Do you get disturbed by imagining the phobic conditions or objects? [ ]
- Do you have fear of losing control in phobic condition? [ ]
- Do you feel shortness of breath in phobic condition? [ ]
TWIN STUDY METHOD

Twin studies have long been used to detangle the role of genetic and environmental factors in the etiology of physiological disorders. For irrational fears and their phobias, epidemiological studies on mono and dizygotic twins suggest significant genetic effect on the onset and prevalence of these disorders. However, the validity of the twin method depends on the equal environment assumption that monozygotic and dizygotic twins are equally correlated in their exposure to environmental factors of etiological importance for the disorder under study. Shared environmental effect contribute to a general susceptibility for phobias, genetic and non-shared environmental effect on the other hand, contribute both to the general susceptibility and specific fearfulness.

The aim of the study was to investigate the genetic and environmental contributions to five phobic fears, and to relate the findings to contemporary theories about the etiology of common phobic fears.

The phobia types which were selected were same on which the general population and community studies were done. However twins were randomly selected from general population of Northern India. Their zygosities were confirmed from the hospital record, keen observation, their physical features i.e. skin complexion, hair colour and texture, eye colour, height etc.

In order to be diagnosed as monozygotic twins, the pair had to exhibit a striking similarity in appearance, so much so that twins are or have often been mistaken for each other, height, finger print pattern count, and finger tip ridge count had to be similar in monozygotic twins. Besides the pair had to be essentially identical in hair colour, hair texture, and hair form, as well as eye colour, eye pigment and iris pattern.
Then skin needed to be of the some complexion (unless one was changed by tanning) and their skin had to display the same amount of body hair distribution on the face, neck and hands. More importantly the pair had to have virtually the same facial features, types of teeth, irregularities in dentition as well as similarities in the size and shape of the hands and fingers. With most of the twins in the test, the details in their palm and finger patterns showed that one hand of one identical in a monozygotic pair was more similar to one of the other twin's hand than to the individual's own opposite hand. In other words, the twin exhibited stronger cross resemblance than internal resemblance in their finger and palm pattern. This peculiar phenomenon among identical twins is commonly referred to as reversed asymmetry or minor imaging. If division of the morula occurs between the teeth and thirteenth days of the development, the twins are commonly found to be mini images of each other. These twins usually demonstrate this minor imaging in hair whorl pattern, deletion, palm and fingertip detail etc, while one twin has whorl going clockwise, the other might have counter clockwise hair whorls.

The genetic contribution heritability to an illness case be estimated by comparing Monozygotic (MZ) Twin can be estimated by comparing Monozygotic Twins with Dizygotic (M Z) Twins. Because monozygotic share all genes while dizygotic twins phase on average only half. Monozygotic twins should be more concordant for a trait with a substantial genetic contribution.

We obtained 5 years apart from two assessments of life history of five unreasonable fears and phobias i.e. bridge and tunnel phobia, traveling (agoraphobia), animal phobia and blood injury phobia (specific type) and glossophobia (social type), from face to face and telephone interviews from 118 individual twin pairs of both mono and dizygotic types including the categories of twins reared apart and reared together. One month apart test retest reliability on 118 twin pairs.

In these twins life time phobias were assessed through semi structured diagnostic interview based on DSM IV-TR criteria and self reported questionnaire, respectively. The positive and negative concordance and discordance regarding the type of phobia, its severity, and age at onset prevalence, comorbidity with other psychoneurotic
disorders were studies in mono and dizygotic twins reared apart and reared together. Dizygotic twins were further assessed for same type of concordance and discordance for same sex and opposite sex members of a pair. The correlations were estimated and heritability in each case was calculated to evaluate the effect of genetic factoring the origin and prevalence of the above mentioned phobias.

**Heritability**

The genetic contribution heritability to an illness case be estimated by comparing Monozygotic (MZ) Twin can be estimated by comparing Monozygotic Twins with Dizygotic (MZ) Twins, Because monozygotic share all genes while dizygotic twins phase on average only half. Monozygotic twins should be more concordant for a trait with a substantial genetic contribution. Therefore, the heritabilities were calculated with the help of concordance and discordance rate of monozygotic and dizygotic twins (for each of the five types of phobias studies here) using the following formula-

\[
\text{Heritability (H)} = \frac{\% \text{ monozygotic concordance} - \% \text{ dizygotic concordance}}{100 - \% \text{ dizygotic concordance}}
\]
OBSERVATION AND RESULTS

Most of the anxiety disorders including the phobic anxieties fall under the category of complex genetic traits which cause mild to moderate to sometimes severe illness in the sufferers. These are those psychoneurotic disorders which are mostly studied by psychologists and psychiatrists but not by very many geneticists perhaps due to the reason that these are not properly following the Mendelian trend of inheritance. Like other complex genetic traits phobias are also reported to be influenced by a number of environmental and/or genetic stresses that generally control their penetrance and expressivity within a population. These environmental factors can be physical (non biological in origin), biological (other individuals and products of other genes within the same individual) or both. Therefore the phenotypic variations seen among the phobia sufferers are genetic as well as environmental contributions. The task of a psychiatric geneticists is therefore to find out that how much of the variation in phenotypes is due to genetical differences like the mechanism of gene expression, nature of the genes involved (dominant or recessive) and the possible mode of inheritance, and how much is due to environmental influence. These were therefore the main goals of the present study and for this the methods of pedigree analysis, sibship comparisons and twin studies were adopted.

Three main classes of phobias i.e. Agoraphobia, specific phobia and social phobia were selected. Out of these Agoraphobia is represented here by the Bridge and elevator phobia, and the other phobia of Tunnel and Enclosed places, while from specific phobia the animal phobia and blood injury phobia are selected and the social phobia is represented by Glossophobia (phobia of speaking in public).

The above mentioned phobic anxieties were studied in two samples. i.e. community sample and general population sample to ascertain proper comparative analysis of these phobic fears. A series of sufferer probands for different phobia types were selected on the basis of age at onset and gender. All of these were showing symptoms according to DSM-IV criteria for respective phobias.
### Table A1- Showing the age at onset in different types of phobias in community and general population sample

<table>
<thead>
<tr>
<th>Types of phobia</th>
<th>Community Sample</th>
<th>General population sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average age at onset in sufferer males</td>
<td>Average age at onset in sufferer males</td>
</tr>
<tr>
<td></td>
<td>Average age at onset in sufferer females</td>
<td>Average age at onset in sufferer females</td>
</tr>
<tr>
<td><strong>Agoraphobia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bridge and elevator</td>
<td>12.3 years</td>
<td>18.1 years</td>
</tr>
<tr>
<td>phobia</td>
<td>10.1 years</td>
<td>14.7 years</td>
</tr>
<tr>
<td>Tunnel and enclosed</td>
<td>6.2 years</td>
<td>6.8 years</td>
</tr>
<tr>
<td>places</td>
<td>5.6 years</td>
<td>6.1 years</td>
</tr>
<tr>
<td><strong>Specific Phobia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Animal phobia</td>
<td>7.2 years</td>
<td>8.4 years</td>
</tr>
<tr>
<td></td>
<td>6 years</td>
<td>6.6 years</td>
</tr>
<tr>
<td>Blood phobia</td>
<td>7.4 years</td>
<td>9.2 years</td>
</tr>
<tr>
<td></td>
<td>6.2 years</td>
<td>6.8 years</td>
</tr>
<tr>
<td><strong>Social phobia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Public speaking</td>
<td>13.2 years</td>
<td>15.5 years</td>
</tr>
<tr>
<td>(Glossophobia)</td>
<td>11.7 years</td>
<td>12.7 years</td>
</tr>
</tbody>
</table>
Table P1- showing the prevalence period of different phobias in community and general population samples.

<table>
<thead>
<tr>
<th>Types of Phobia</th>
<th>Community Sample</th>
<th>General population sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percentage of sufferers showing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prevalence of one year or less</td>
<td>Prevalence of one to five years</td>
</tr>
<tr>
<td>Bridge and elevator</td>
<td>53.78%</td>
<td>37.35%</td>
</tr>
<tr>
<td>Tunnel &amp; enclosed places</td>
<td>7.86%</td>
<td>51.46%</td>
</tr>
<tr>
<td>Animal phobia</td>
<td>20.36%</td>
<td>56.13%</td>
</tr>
<tr>
<td>Blood phobia</td>
<td>28.15%</td>
<td>44.09%</td>
</tr>
<tr>
<td>Glossoaphobia</td>
<td>11.08%</td>
<td>74.82%</td>
</tr>
</tbody>
</table>
Table AB1 - Showing consolidated data of sufferers and non-sufferers for all the Phobic Anxieties studied in the present survey.

<table>
<thead>
<tr>
<th>Phobia types</th>
<th>No. of pedigrees</th>
<th>No. of Total individuals</th>
<th>Percentage of Sufferers/Non sufferers</th>
<th>Percentage of sufferers male/female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Community samples</td>
<td>General samples</td>
<td>Community samples</td>
<td>General samples</td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>Community samples</td>
<td>General samples</td>
<td>61</td>
<td>61</td>
</tr>
<tr>
<td>Bridge &amp; Elevator Phobia</td>
<td>Community samples</td>
<td>General samples</td>
<td>43</td>
<td>39</td>
</tr>
<tr>
<td>Tunnel &amp; Enclosed Places Phobia</td>
<td>Community samples</td>
<td>General samples</td>
<td>145</td>
<td>141</td>
</tr>
<tr>
<td>Specific Phobia</td>
<td>Community samples</td>
<td>General samples</td>
<td>80</td>
<td>77</td>
</tr>
<tr>
<td>Animal Phobia</td>
<td>Community samples</td>
<td>General samples</td>
<td>49</td>
<td>47</td>
</tr>
<tr>
<td>Blood Phobia</td>
<td>Community samples</td>
<td>General samples</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Phobia</td>
<td>Community samples</td>
<td>General samples</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glossophobia</td>
<td>Community samples</td>
<td>General samples</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>