# Suicidal Behaviour in Context of Mood Disorders

# Outline

- Introduction
- Epidemiology
- Risk factors
- Antidepressant associated suicidal behaviour
- Prevention
- Summary

# Introduction

- Suicidal behaviour - one of the most alarming signs and most common reasons for contact with medical services, esp. psychiatry services
- Multicausal – medical, biological, psychosocial, demographic & cultural components, familial–genetic disorders, personality, psychosocial
- Better understanding on what makes the minority of pts. with mood disorders suicidal

# Epidemiology

- >800,000 people die by suicide; >20 million attempt suicide each year
- Accounts for 1.4% of all deaths worldwide (15th leading cause of death)
- Underreported/misclassified statistics
- Annual global suicide rates: Males – 15, Females – 8, General population – 11.4 per 100,00 population
- Suicides account for 52% and 71% of all violent deaths in males and females respectively
- 15-29 yrs. age group – 2nd leading cause of death (8.5% of all deaths)

# Epidemiology

- Suicide- 10$^{th}$ most common cause of mortality in general population in well-developed countries
- 90% suicide victims – at least one (mostly untreated) major psychiatric disorder at the time of their death
- 50-66% - major mood disorder (depression) ± anxiety & personality disorder
- Attempted : Completed suicide = 15-40:1; 5-10:1 in major mood disorder (lethal/violent methods used) and BPD

# Epidemiology

- ~50% of those who complete suicide have attempted suicide at least once previously
- 1st attempt significantly increases the risk of future completed suicide
- ~ 20 % of those who attempt suicide eventually will die by their own hand
- Individuals who repeatedly attempt suicide switch from nonviolent/nonlethal methods to violent/lethal methods

# Epidemiology

- 10-18% adults in general population worldwide report lifetime suicidal ideation
- 3-5% - at least one suicide attempt
- Prior suicide attempt and current major depression - strongest predictors of future suicide
- Standardized mortality ratio of suicide death in patients with major mood disorders (UPD & BPD) is 10-30 times that of general population

# Epidemiology

- Lifetime risk of completed suicide in US in:
  - General population – 0.5%
  - Non-suicidal major depressive outpatients – 2.2%
  - Major depressive inpatients hospitalized without specification of suicidality – 4.0%
  - Severe major depressives hospitalized for suicidality – 8.6%

# Epidemiology

- Denmark study: pts. Born b/w 1955-1991, treated in psychiatric hospital up to 2006, absolute lifetime risks of completed suicide:
  - BPD: Males – 7.8% Females – 4.8%
  - UPD: Males 6.7% Females – 3.8%
- Finland study (1997-2003): Pts. Hospitalized due to severe suicide attempts (N = 23,321) , mood disorders (N = 5,164) raised risk of completed suicide by 72% and suicide attempt by 59% during mean follow up time of 3.6 years

# Epidemiology

- Other long-term follow-up studies: Rate of completed suicide higher in BPD than UPD
- More than 50% of BPD and 33% of UPD have had one or more suicide attempts; Suicidal ideation more common
- Rates of previous suicide attempts in:
  - UPD: 13%
  - BPD-I: 28%
  - BPD-II: 33% (cyclothymic affective temperament)

# Epidemiology

- Risk of completed and attempted suicide in BPD is higher in younger ages
- BPD with past suicide attempts have earlier age at onset

# Suicide Risk Factors

**Illness related risk factors**

- Risk factors related to current mood episodes
  - Severe major depressive episode
  - Major depressive/manic episodes with mixed features
- Risk factors related to prior course of mood disorders

**Personality related & historical risk factors**

- Risk factors related to personality features
- Risk factors related to personal history/family history

# Biological Risk Factors

- Decreased (dysregulated) central serotonergic; related to impulsive-aggressive personality; Low levels of 5-HIAA found in CSF
- Increases chances of suicidal behaviour, esp. in acute episodes of major psychiatric disorder and adverse psychosocial situations
- Others:
  - Tryptophan Hydroxylases TPH1 & TPH2,
  - Serotonin Transporter 5-HTT (SLC6A4 gene)
  - Serotonin Receptors (HTR1A, HTR1B, HTR2A, HTR2C, etc.)
  - Monoamine Oxidases–MAOA and MAOB

# Biological Risk Factors

- Dopaminergic pathway also implicated:
  - Catechol-O-Methyltransferase
  - Dopamine Receptor DRD2
- Hyperactivity of hypothalamic–pituitary–adrenal axis – predictor of future completed suicide, esp. in major depressive
- Other systems implicated – GABA, NMDA, Cholesterol, Omega-6 & Omega-3 metabolism
- Limited practical value

# Specific Clinical Characteristics of Current Mood Disorder

- Attempted/completed suicides usu. during major depressive or mixed episodes (75%), rarely during (hypo)mania/euthymia
- Suicidal behaviour - state & severity dependent
- Earlier age of onset, higher frequency of mood episodes (rapid cycling course), comorbid anxiety disorder and substance use
- Predisposing factors interact with precipitating stressors
- Deaths, separations, and other major losses, scandals, or imprisonment rarely precipitate suicide in absence of a psychiatric disorder.

# Specific Clinical Characteristics of Current Mood Disorder

- Depression of suicide victims differs qualitatively from that of living depressed controls:
  - Severity – insomnia, hopelessness, worthlessness, inappropriate guilt, death wishes/suicidal ideation anxiety, agitation, weight/appetite loss
  - Volatile & erratic moods a/w dysphoria & agitation or who have mixed states
  - Psychotic features
- Minor depression & pure dysthymic disorder do not markedly increase the risk of suicide; may develop major depressive disorder, hence increased suicide risk

# Comorbid Psychiatric, Personality & Medical Disorders

- Mood disorders + comorbid anxiety disorders, substance use disorders, cigarette smoking, personality disorders, any serious, disabling, painful and fatal medical illness - increased risk of attempted/committed suicide.
- Suicidal behaviour: BPD + ADHD > BPD alone
- Chronic alcoholism/acute alcohol intake – triggers actual suicidal behaviour, increases lethality of suicidal acts

# Comorbid Psychiatric, Personality & Medical Disorders

- Cigarette smoking - +vely related to suicidal behaviour in general population and major mood disorders
- Major depression, bipolar disorder & schizophrenia – a/w higher rates of cigarette smoking; significant even after controlling psychiatric morbidity
- Smokers – impulsive; smokers with major depressive disorder – greater number of depressive symptoms and higher levels of suicidality during depressive episode
- Disabling, painful, and/or life-threating medical disorders, including cancer, are also at elevated risk of suicide, esp. in presence of depression

# Prior Course of Mood Disorders

- Early onset of UPD/BPD
- Relatively early stage of the illness,
- First episode depression
- Predominantly depressed polarity during prior course of the illness(BPD-II)
- Rapid cycling bipolar disorder
- Suicidal ideation/suicide attempt in the past

# Specific Personality Features

- Impulsivity, aggressivity, pessimism
- Strong association b/w impulsiveness and BPD – becomes more pronounced during depressive/(hypo)manic episodes
- Hyperthymic temperament/Cyclothymic, irritable or depressive affective temperaments – characteristic for BPD (II) - increased suicidal risk for both BPD & UPD
- Cyclothymic temperament predisposes to future BPD transformation and suicide attempts in adult and juvenile depressives
- BPD-I, II, UPD with cyclothymic temperament - higher rate of prior suicide attempts lifetime/current suicidal ideation

# Specific Personality Features

- Marked affective temperaments (15-20% general population) – higher chances of developing major mood disorders - suicide risk factor
- Cyclothymic/irritable affective temperament – childhood physical and/or sexual abuse
- Pessimistic personality features, cognitive rigidity, ruminative thinking, maladaptive coping strategies, and disturbed neurocognitive functions
- Stress-diathesis model: suicidal behaviour is determined by both stressor (acute major psychiatric illness or acute major personal crisis) and diathesis/predisposition (impulsive, aggressive, pessimistic personality traits)

# Previous Suicide Attempts

- Most powerful single predictor of future attempts and fatal suicide, esp previous use of violent/lethal methods
- 33% of UPD and 50% of BPD attempt suicide at least once during their lifetime (consistent among major depressive episodes)
- Suicidal depressives frequently become suicidal again in the next depressive episode

# Previous Suicide Attempts

- BPD (II) v/s UPD – use more violent/lethal suicide methods patients (males)
- Pts. repeatedly attempting suicide switch over to violent/lethal methods; reversal rare
- BPD-D + h/o suicide attempts – severe symptomatology  - more hopelessness, self-blame, guilt, suicidal ideation, aggressive-impulsive personality traits

# Family History of Suicidal Behaviour

- +ve family history in 1st and 2nd degree relatives - one of the strongest risk factors
- Heritability index of completed suicide – 40%; higher among depression-related suicides
- Familial component of suicidal behaviour - partly independent of specific psychiatric disorders - relatives of suicidal persons 10 times more likely to show SI
- Children of parents with mood disorders + suicide – 5 times more likely to attempt even after controlling offspring risk factors

# Family History of Suicidal Behaviour

- BPD-D & UPD with f/h/o suicidal behaviour, childhood physical/sexual abuse – higher risk
- Several components:
    - Genetic background of major psychiatric disorders
    - Genetic–familial nature of impulsive-aggressive personality traits irrespective from psychiatric disorder
    - Copycat mechanisms.
- "Suggestive" effect of suicidal family member becomes active when major depressive or other severe mental disorder develops

# Negative Life Events and Adverse Life Situations

- Trigger suicidal behavior in vulnerable, high-risk persons (major depression)
- Adverse, unwanted, or stressful life events act as:
  - predisposing (childhood events, including physical and sexual abuse)
  - precipitating (adulthood events) factors.
- 33% UPD/BPD pts. – h/o childhood physical and/or sexual abuse/neglect – earlier age of onset, greater psychiatric comorbidities, higher rates of suicide attempts and

# Negative Life Events and Adverse Life Situations

- Developmental and neuroendocrinological scars – make the subject vulnerable for suicidal behaviour in a crisis situation
- Ability to regulate affect gradually acquired after birth, requires reasonable parenting (Affect mastery)
- Developmental stages – different emotional stresses – children learn to deal with separations, frustrations and other emotionally challenging circumstances – "secure attachment" necessary
- Frightened/Insecure/Vindictive parent – prevents child from making "secure attachment"
- Insecure attachment + affective dysregulation – suicide risk

# Negative Life Events and Adverse Life Situations

- 50% of completed suicides in BPD/UPD - a/w recent severe, acute, negative life events, adverse life situations, isolation, living alone, separated/divorced/unmarried
- (Hypo)manic episodes – over expenditure, aggressive–impulsive behavior, or episodic promiscuity – IPR conflicts, marital breakdown, new –ve life events – negative impact – trigger a new depressive episode/suicidal behaviour
- Other relevant stressful events: IPR conflicts, occupational difficulties, personal/economic losses, retirement, bereavement, social isolation, feeling stigmatized limited access to support or health care or social services

# Negative Life Events and Adverse Life Situations

- Permanent adverse life situations (e.g., unemployment and social isolation) and acute psychosocial stressors (e.g., loss events and financial breakdowns) in adult patients with UPD/BPD – indicators of suicidality
- High suicide risk very high in
  - 1st few days of hospitalization
  - Few days-weeks after discharge (esp. unplanned)
  - Short hospital stay
  - Numerous previous hospitalization
  - Lack of follow-ups

# Demographic Factors

- Females and young persons more commonly attempt suicide.
- Suicide mortality is elevated in veterans, health care professionals, and agricultural workers.
- Less pronounced role – do not have a clinically significant predictive value in UPD/BPD
- Close relatives of suicide victims – high risk of suicidal behaviour; require professional help immediately after suicide of their relative
- Peak during spring & early summer, low during winters; more pronounced among depression, males and violent means

# Clinical Utility of Suicide Risk Factors

American Association of Suicidology: “Is Path Warm”

- I - Ideation—threatened or communicated
- S - Substance abuse—excessive or increased
- P - Purposeless—no reasons for living; anhedonia
- A - Anxiety, agitation and insomnia
- T - Trapped—feeling no way out; perceived burdensomeness
- H - Hopelessness
- W - Withdrawal—from friends, family, society
- A - Anger (uncontrolled)—rage, seeking revenge
- R - Recklessness—risky acts, unthinking
- M - Mood changes (dramatic)

# Suicide Protective Factors

- Good family and social support
- Pregnancy & postpartum period
- Large number of children
- Strong religious beliefs
- Regular physical activity
- Restricting lethal suicide methods
- Stricter laws on drug and gun control
- Optimistic personality features
- Hyperthymic temperament
- Acute and long-term treatment, (non)pharmacological

# Antidepressant Associated Suicidal Behaviour

- 2004 - FDA – 24 short term placebo-controlled trials of antidepressants in child and adolescent MDD, OCD and other psychiatric disorders – risk of suicidality (suicidal thinking & behaviour) was 4% - twice the placebo rate
- Black box warning added to antidepressants
- Paradox
- Later meta-analysis of 27 trials of paediatric major depression, risk of suicidality was 3% in antidepressant group and 2% in placebo

# Antidepressant Associated Suicidal Behaviour

- Absolute rate of response in antidepressants – 61%, placebo – 50%
- Number needed to treat (NNT) – 10; Number needed to harm - 112
- Benefits of antidepressants in youths outweigh the potential risk from suicidal ideation or attempts.

# Antidepressant Associated Suicidal Behaviour

- Cause: Lack of antidepressant effect; suicide-inducing potential rare (antidepressants can sometimes worsen depression)
- Unrecognized BPD-D (BPD-II) & mixed UPD with intradepressive (hypo)manic symptoms in RCTs on antidepressant monotherapy are considered UPD; receive antidepressants ± anxiolytics but no mood stabilizers
- Antidepressant monotherapy without mood stabilizers/SGA in (sub)threshold BPD-D with early age of onset and young current age – antidepressant resistance –may worsen depression by causing (hypo)mania switch or inducing/aggravating depressive mixed state/agitation – "Activation Syndrome" – more common in BPD

# Antidepressant Associated Suicidal Behaviour

- 2004 - FDA Black Box Warning – decreased use of antidepressants in children and adolescents a/w increased suicide rates in those age groups
- Need for precise and early diagnosis of BPD, even first-episode depressives, and the formal recognition of bipolar depressive mixed states will help to identify pseudounipolar mixed depressives for whom antidepressant monotherapy is contraindicated and for whom mood stabilizers and/or atypical antipsychotics are indicated on clinical grounds.

# Prevention of Suicide

- Majority of suicide attempts and completed suicides in patients with mood disorders are preventable
- Reduce time spent in major depressive or mixed affective episode
- Adequate long term therapy essential
- Acute suicide danger - close observation & urgent hospitalization
- Crisis intervention
- Hospitalization as short as possible

# Prevention of Suicide

- Eliminating acute suicide danger
- Improving early diagnosis and treatment of mood disorders (subthreshold BPD)
- Improving compliance (psychoeducation, psychotherapy, CBT)
- Educating public via printed and electronic media

# Prevention of Suicide

- Not hospitalized – close observation and removing possible means of suicide
- Treatment of anxiety, psychomotor agitation and insomnia – increase suicide risk
- ECT – severe suicidal behaviour (stupor/catatonia)
- Acute and long-term pharmacotherapy (antidepressants in UPD and mood stabilizers in BPD) markedly reduces suicide morbidity and mortality

# Prevention of Suicide

- BPD on mood stabilizers (Lithium > AED) (with)out antidepressants/antipsychotics & UPD on antidepressants, 70-80 % risk reduction of completed and attempted suicide compared to those without pharmacological treatment
- Lithium nonresponse in pts with suicide risk factors – retain lithium and add another mood stabilizer
- Suicide rates through "anti-depressant" era (1960-92) progressively decreased

# Prevention of Suicide

- Add anxiolytics, atypical antipsychotics, and sleep-promoting drugs
- Ketamine – rapidly reduces current suicide risk
- Depression-focused psychotherapies + pharmacotherapy – improves compliance, increases effectiveness of pharmacotherapy
- Hopelessness–pessimism & aggressiveness–impulsiveness: CBT + pharmacotherapy

# Prevention of Suicide

- Improving the patients compliance via psychoeducation, psychotherapy and cognitive behaviour therapy
- Educating the public about the symptoms, dangers and treatable nature of mood disorders and the preventable nature of suicidal behaviour
- Reducing the stigma against mood disorders and suicide
- Providing information on how and where to get help in case of mood disorders and suicide crisis

# Summary

- Clinicians should be aware of communications about suicide
- Pts. talk about suicide, death, and/or having no reason to live often
- Definite warnings of their suicidal intentions, but caregivers are unaware/do not know how to respond
- Suicidal intent - sometimes denied/minimized.
- Clinicians should always remember to ask about suicide
- Questioning patients about suicide thoughts and plans - always indicated and crucial for proper prevention.
- Talking about suicide does not increase the risk

# Summary

- Early recognition of bipolar nature of depressive disorders in order to prevent delay in initiation of mood stabilizers
- Adequate short-term & long-term treatment
- Early detection of suicidal risk and plan prevention strategies as early as possible even before the 1st suicidal act

# References


- Kaplan HI. Kaplan & Sadock's Comprehensive Textbook of Psychiatry, (2 Volume Set, 2017).
- Zai CC, de Luca V, Strauss J, Tong RP, Sakinofsky I, Kennedy JL. 11 Genetic Factors and Suicidal Behavior. The neurobiological basis of suicide. 2012 Jun 25:213.

# Thank You